Studies on Nickel-Catalyzed Cyanofunctionalization of Alkynes and Dienes(Dissertation_全文)

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Contents

Abbreviations

Ac	acetyl
aq.	aqueous
Ar	aryl
atm	atmospheric pressure
binap	2,2’-bis(diphenylphosphino)-1,1’-binaphtyl
Bn	benzyl
br	broad
Bu	butyl
ca.	about(circa)
cat.	catalyst
cf.	confer
cod	1,5-cyclooctadiene
conc.	concentrated
Cp	cyclopentadienyl
Cy	cyclohexyl
d	doublet
δ	scale (NMR)
DIBAL-H	diisobutylaluminium-hydride
DMF	*N*,*N*-dimethylformamide
DMSO	dimethyl sulfoxide
DPEphos	bis[2-(diphenylphosphino)-phenyl]ether
dppb	1,4-bis(diphenylphosphino)-butane
dppf	1,1’-bis(diphenylphosphino)-ferrocene
dppp	1,3-bis(diphenylphosphino)-propane
dpppent	1,5-bis(diphenylphosphino)-pentane
dpphex	1,6-bis(diphenylphosphino)-hexane
dr	diasteremeric ratio
ebi	ethylenebis(1-indenyl)
ee	enantiomeric excess
EI	electron ionization
eq.	equation
equiv	equivalent
Et	ethyl
FAB	fast atom bombardment
FG	functional group
FID	flame ionization detector
GC	gas chromatography
GPC	gel permeation chromatography
h	hour(s)
Hex	hexyl
HMBC	hetero-nuclear multiple-bond connectivity
HRMS	high-resolution mass spectra
Hz	hertz
i	iso
IR	infrared spectroscopy
J	copling constant

L	ligand	quant	quantitative
LAH	lithium aluminum hydride	quint	quintet
LUMO	lowest unoccupied molecular orbital	ref.	reference
		rt	room temperature
M(m)	metal	s	singlet
MAO	methylaluminoxane	sept	septet
Me	methyl	sext	sextet
min	minute(s)	t	triplet
mL	milliliter	*t*, *tert*	tertiary
μL	microliter	TBAF	tetrabutylammonium fluoride
mp	melting point		
n	normal	Temp.	temperature
NMR	nuclear magnetic resonance	THF	tetrahydrofuran
NOE	nuclear Overhauser effect	TIPS	triisopropylsilyl
Pent	pentyl	TLC	thin layer chromatography
Ph	phenyl	tol	tolyl
Phth	phthalimide	UV	ultraviolet
pin	pinacolato	*vic*	vicinal
PMHS	polymethylhydrosiloxane	wt%	weight percent
Pr	propyl	Xantphos	9,9-dimethyl-4,5-bis-(diphenylphosphino)xantene
q	quartet		

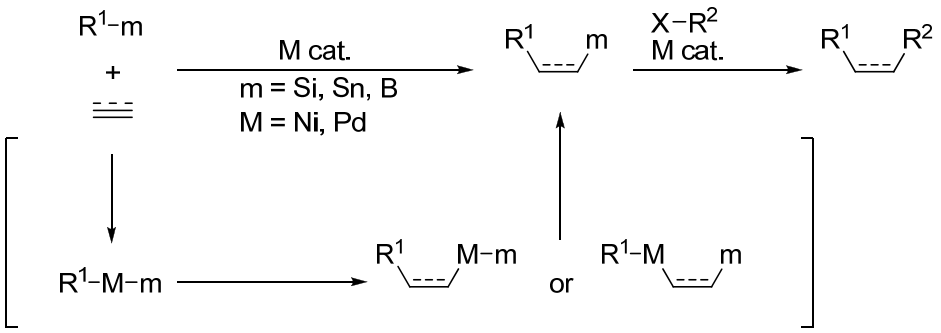
Chapter 1

Introduction and General Summary

In view that all natural products, pharmaceuticals, agrochemicals, and organic materials consist of carbon frameworks, development of new carbon–carbon (C–C) bond forming reactions with efficiency higher than ever achieved is an important issue in modern organic synthesis. In order to construct C–C bonds, nucleophilic addition reactions to polar C=X (X = C, O, NR, etc.) bonds, nucleophilic and electrophilic substitution, rearrangement, and pericyclic, and radical reactions have been playing key roles in modern organic synthesis.[1] However, chemo-, regio-, and/or stereoselectivities associated with these reactions are not always satisfactory to achieve truly efficient organic synthesis. Accordingly, attention has been focused on transition metal catalysis, and significant progress has been made in the last four decades to allow a diverse range of regio-, stereo-, and chemoselective C–C bond formations, which were inaccessible by classic methodologies.[2] Especially, transition metal-catalyzed addition reactions of element–element bonds across C–C unsaturated bonds are highly useful because the reaction allows us to achieve regio- and stereoselective construction of two carbon–element bonds at the same time without forming byproducts.[3]

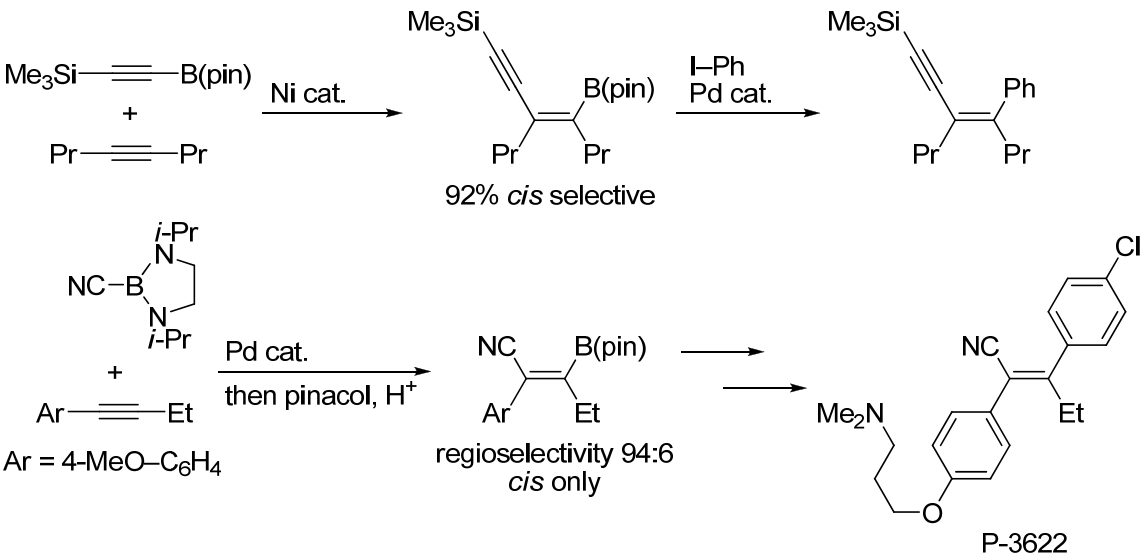
Transition metal-catalyzed carbometalation of unsaturated bonds followed by cross-coupling reactions

Among various addition reactions catalyzed by transition metal complexes, addition reactions of less nucleophilic main group organometallic reagents such as organoboranes, -silanes, and -stannanes across unsaturated C–C bonds, namely, carbometalation reactions, are particularly useful, because such transformation allows simultaneous formation of both C–C and C–m (m = B, Si, Sn) bonds in a single operation (Scheme 1). The resulting C–m bonds can be further transformed to various C–C bonds by metal-catalyzed reactions such as cross-coupling and carbonyl addition reaction in a highly chemoselective and stereospecific manner.[2] Therefore, these two-step transformations serve as a useful method for regio-, stereo-, and chemoselective introduction of two organic groups to unsaturated C–C bonds. The carbometalation reaction is generally initiated by oxidative addition of R^1–m bonds to transition metal complexes. The following insertion of unsaturated bonds into the R^1–M or M–m bond and reductive elimination afford carbometalation products in a highly stereospecific *cis* manner and regenerate the metal catalysts.



Scheme 1. Carbometalation of unsaturated C–C bonds followed by cross-coupling.

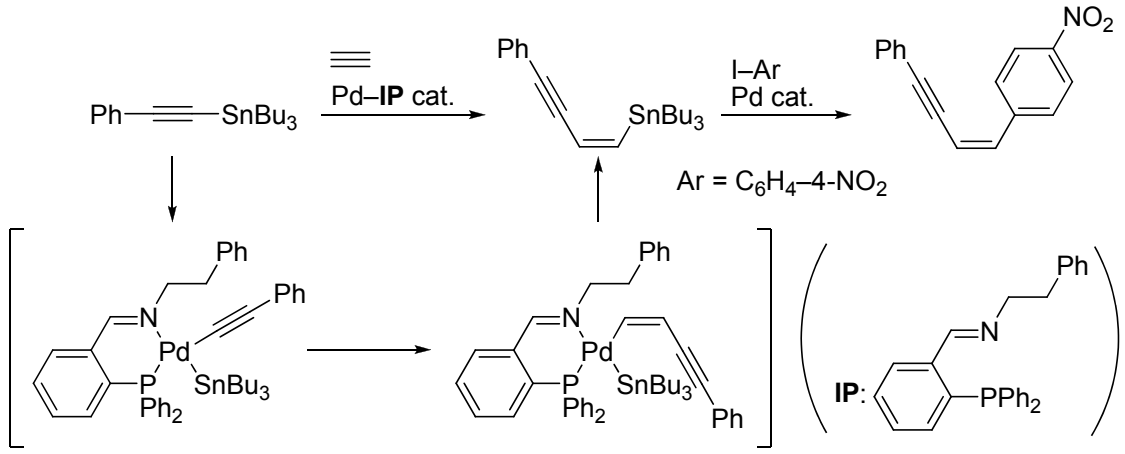
For example, carboboration reactions via cleavage of C(sp)–B bonds followed by insertion of alkynes to give stereo- and regiochemically defined alkenylboronic acid esters have been achieved with nickel or palladium catalysts.[4] Further C–C bond formation is achieved by palladium-catalyzed cross-coupling reaction with aryl halides to afford tetra-substituted ethenes such as P-3622, a potential squalene synthetase inhibitor (Scheme 2).



Scheme 2. Carboboration of alkynes followed by cross-coupling reaction.

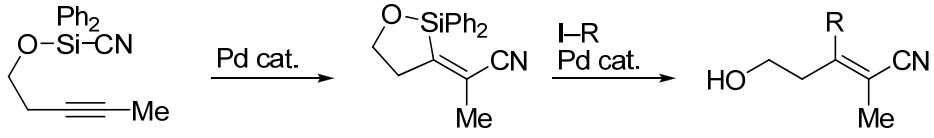
Highly functionalized alkenylstannanes are readily prepared by palladium-catalyzed carbostannylation reactions of alkynes.[5] For example, alkynylstannanes add across alkynes stereoselectively in the presence of a

palladium/iminophosphine catalyst to give alkenylstannanes having a conjugated enyne substructure. This reaction is also initiated by oxidative addition of C(sp)–Sn bonds to the palladium complex. The resulting alkenylstannanes can be used as a mild nucleophile for palladium-catalyzed cross-coupling reactions (Scheme 3).



Scheme 3. Carbostannylation of alkynes followed by cross-coupling reaction.

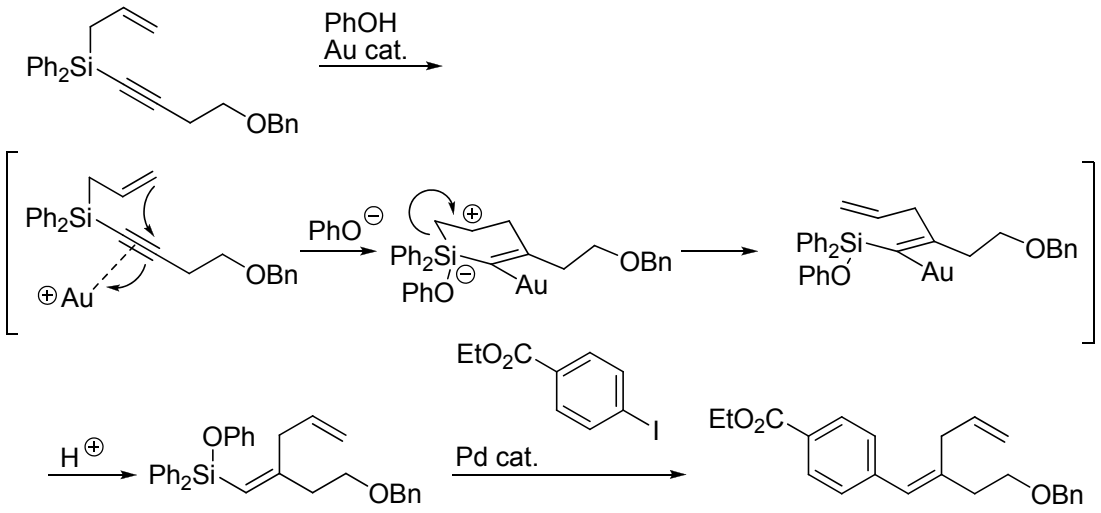
Organosilicon compounds are also useful for chemoselective C–C bond forming reactions.[6] Therefore, carbosilylation of unsaturated compounds should be of synthetic value to prepare organosilicon compounds with a complex structure. Intramolecular silylcyanation of alkynes proceeds under palladium catalysis to afford highly substituted alkenylsilanes, which subsequently undergo cross-coupling reaction to give tri-substituted acrylonitriles (Scheme 4).[7d]



Scheme 4. Intramolecular cyanosilylation of alkynes followed by cross-coupling reaction.

Inter- and intramolecular allylsilylation reactions of alkynes are catalyzed by gold, aluminum, or hafnium. These Lewis acid catalysts are considered to activate alkynes to induce sila-Cope rearrangement which proceeds through intramolecular allylsilylation

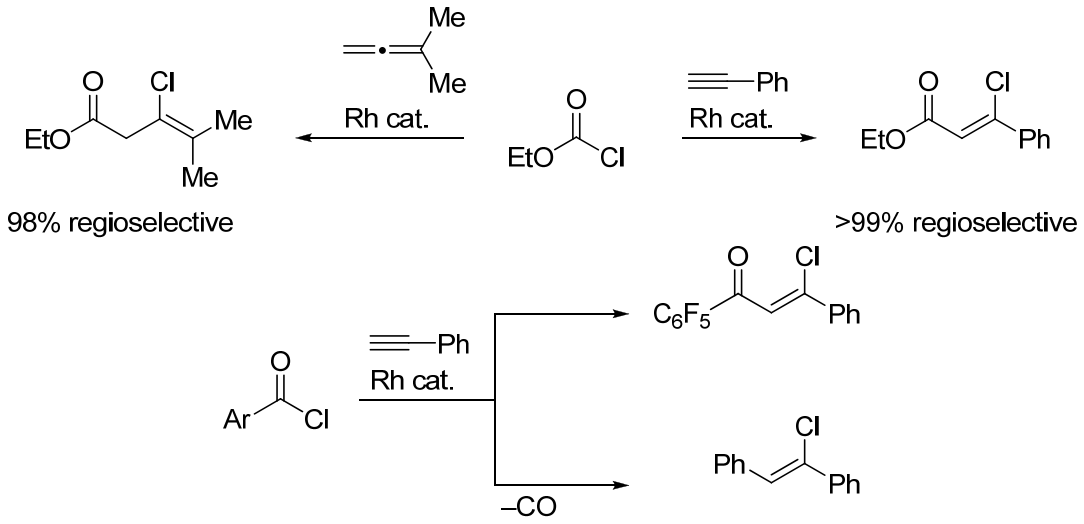
of alkynes.[8] The resulting alkenylsilanes thus obtained also undergo the palladium-catalyzed cross-coupling reaction with aryl iodides (Scheme 5).[8g]



Scheme 5. Gold-catalyzed allylsilylation of alkynes followed by cross-coupling reaction.

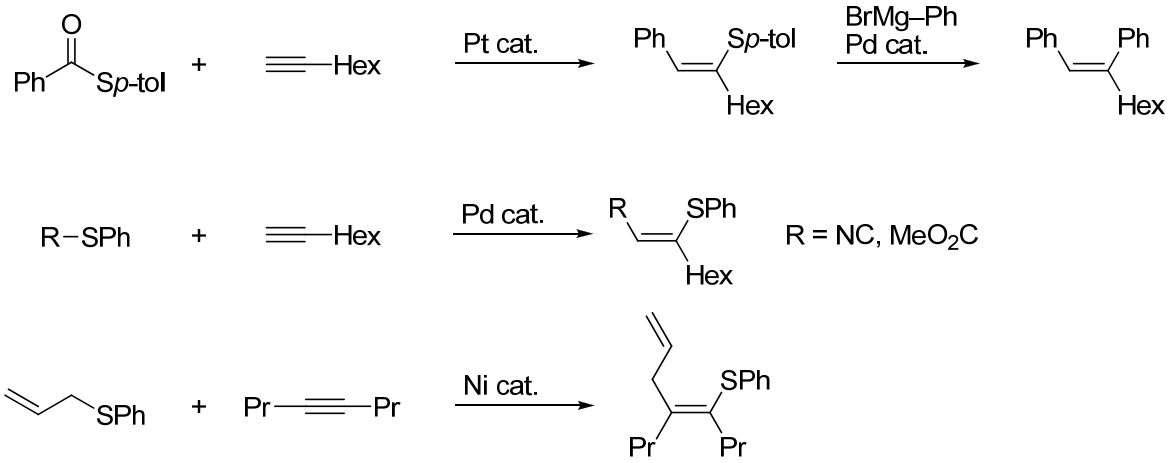
Carbohalogenation and carbochalcogenation of unsaturated C–C bonds followed by cross-coupling reactions

Transition metal-catalyzed carbohalogenation reaction of unsaturated C–C bonds followed by transformations of the resulting C–X (X = halogen) bonds is an alternative strategy to doubly functionalize unsaturated bonds. Rhodium-catalyzed regio- and stereoselective chloroesterifications of alkynes and 1,2-dienes have been reported to give highly functionalized alkenyl chlorides.[9b,c] Electron-deficient aroyl chlorides also add across terminal alkynes with a rhodium catalyst,[9e] whereas decarbonylative arylchlorination takes place with electron-neutral and -rich aroyl chlorides (Scheme 6).[9a,d] These alkenyl chloride may serve as electrophiles for further transformations such as cross-coupling reactions, though not demonstrated.



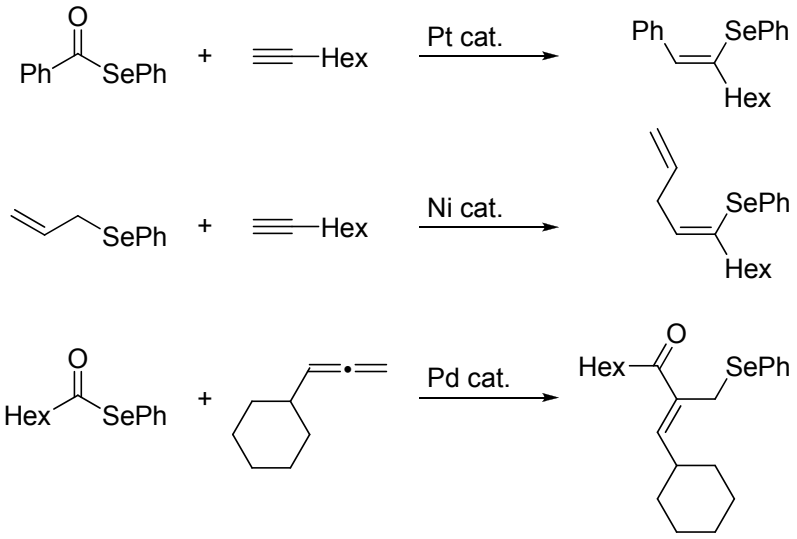
Scheme 6. Carbochlorination of alkynes and 1,2-dienes catalyzed by rhodium.

Carbon–chalcogen bonds can also be activated by transition metal complexes, as exemplified by transition metal-catalyzed carbochalcogenation reactions of unsaturated C–C bonds. For example, platinum-catalyzed decarbonylative carbothiolation followed by cross-coupling reaction with Grignard reagents gives tri-substituted ethenes.[10,11] Thiocyanation,[12] thioesterification,[13] and allylthiolation[14] reactions are also catalyzed by group 10 transition metals to give a range of alkenyl thioethers in stereo- and regioselective manners (Scheme 7).



Scheme 7. Carbothiolation of alkynes catalyzed by group 10 transition metal catalysts.

Related addition reactions using organoselenium reagents across unsaturated bonds are also achieved with group 10 metal catalysts (Scheme 8).[15] These reactions generally proceed regio- and stereoselectively to give highly functionalized organoselenium compounds, which can serve as organic electrophiles for cross-coupling reactions.[10]

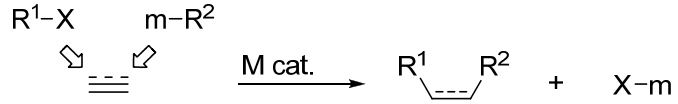


Scheme 8. Carboselenation of unsaturated bonds.

Although the two-step protocols that involve carbometalation, carbochlorination, or carbochalcogenation followed by C–C bond forming reactions such as cross-coupling reactions are useful to introduce two carbonaceous groups into unsaturated compounds, work up and isolation of products are required in general for each step, thus reducing synthetic efficiency.

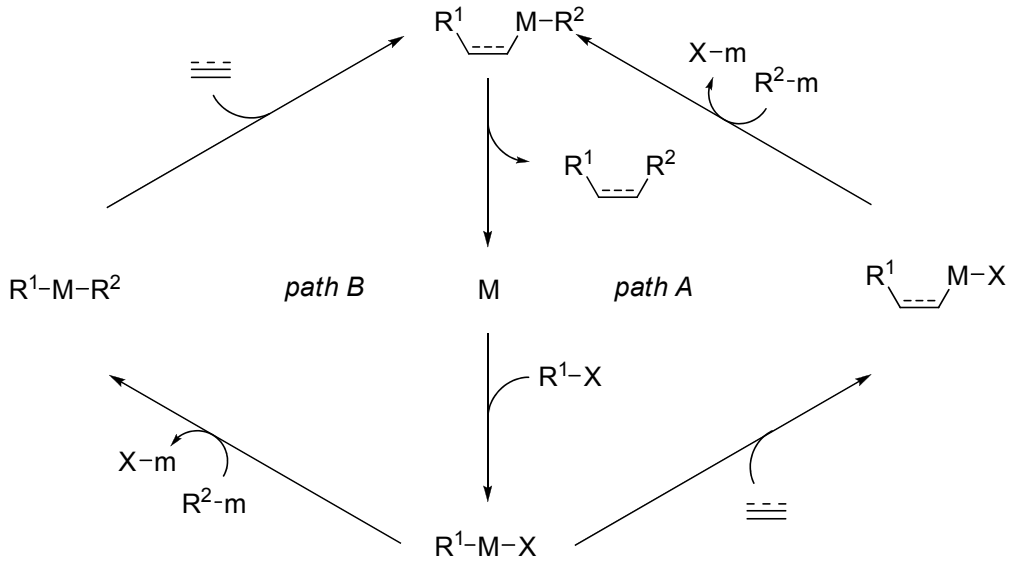
Three-component coupling of organometallic reagents, unsaturated compounds, and organic electrophiles

In principle, introduction of two organic groups into unsaturated bonds in a single operation may be possible by transition metal-catalyzed three-component coupling reactions of carbonaceous nucleophiles, unsaturated C–C bonds, and carbonaceous electrophiles (Scheme 9).[16] There are indeed several examples of this type.



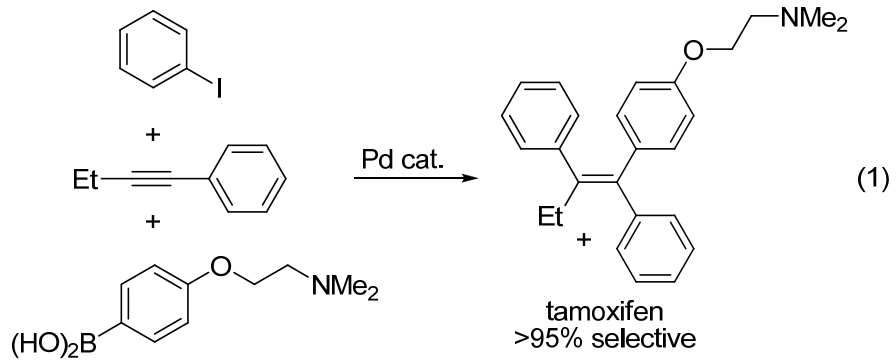
Scheme 9. Three-component coupling of organic halides, unsaturated C–C bonds, and organometallic reagents.

Two reasonable and well-accepted mechanisms of this transformation are shown in Scheme 10. Both catalytic cycles are initiated by oxidative addition of organic halides. Insertion of unsaturated bonds into the R^1–M bond, transmetalation to organometallic reagents R^2–m to generate alkenyl- or alkylmetal intermediates, and reductive elimination afford adducts having two newly formed C–C bonds all in one-pot (Scheme 10, path A). Transmetalation may take place prior to the insertion of unsaturated bonds (Scheme 10, path B).



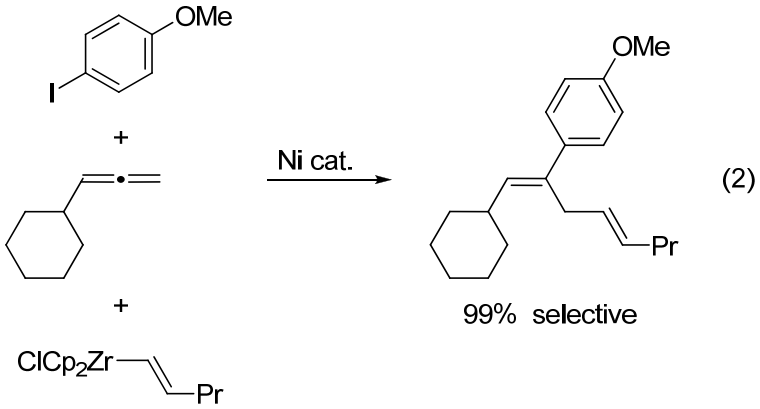
Scheme 10. General catalytic cycle of transition metal-catalyzed three-component coupling.

For example, regio- and stereoselective three-component coupling reaction of aryl halides, internal alkynes, and arylboronic acid is achieved with a palladium catalyst to provide tetra-substituted ethenes such as tamoxifen in a single operation (eq. 1).[17]



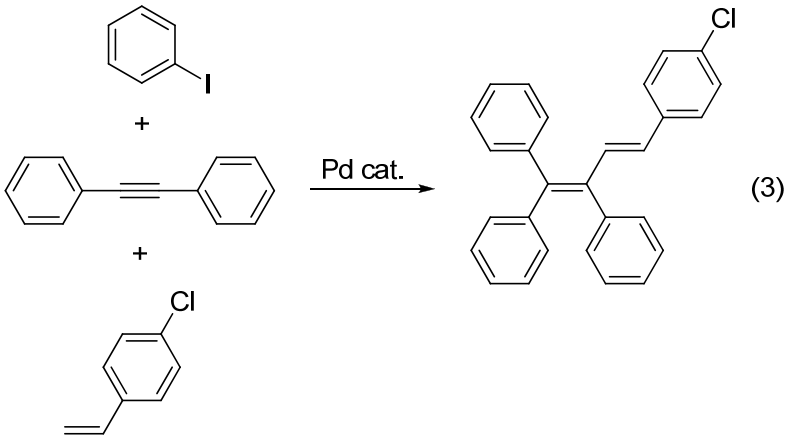
(1)

A similar transformation using 1,2-dienes, alkenylzirconium reagents, and aryl iodides is catalyzed by a nickel complex to give highly substituted 1,4-dienes with high stereo- and regioselectivities (eq. 2).[18]



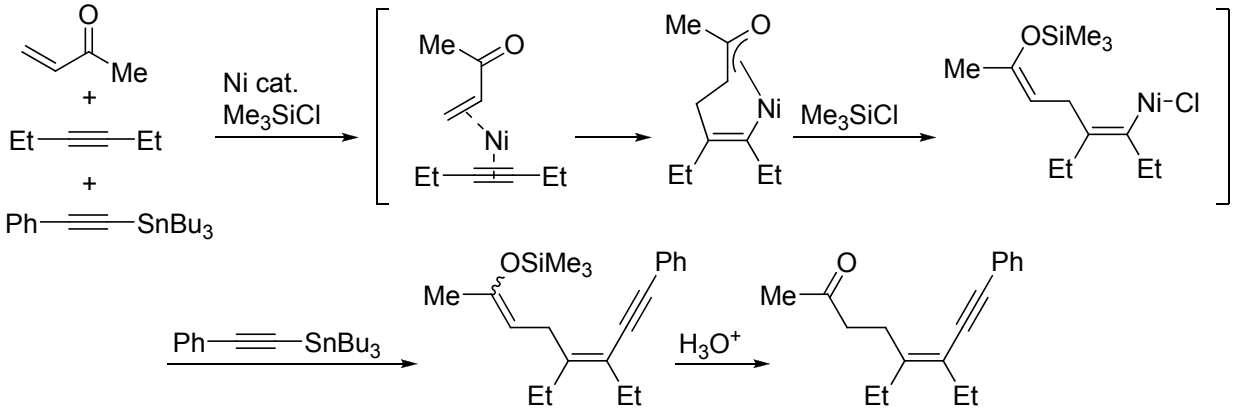
(2)

Vinylarenes can be employed instead of organometalic reagents in stereoselective difunctionalization of alkynes catalyzed by palladium, and tetra-substituted 1,3-butadienes (eq. 3).[19]



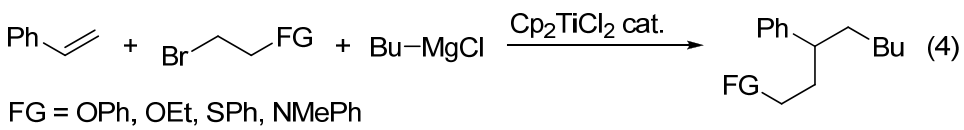
(3)

A combination of enones and chlorosilanes serves as an electrophile for nickel-catalyzed multi-component coupling reactions with alkynes and alkynylstannanes.[20] A reaction mechanism involving formation of oxa-π-allylnickelacycle intermediates followed by transmetalation with alkynylstannanes is proposed to explain the formation of silyl enol ethers, which upon hydrolysis afford highly substituted conjugated enynes (Scheme 11).



Scheme 11. Coupling of enones, chlorosilanes, alkynes, and alkynylstannanes.

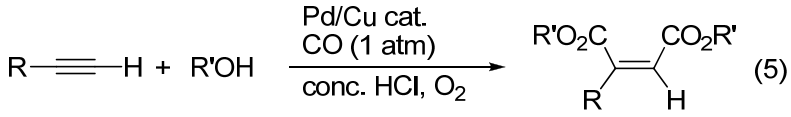
A proper choice of substrate combinations allows regioselective three-component coupling reactions involving radical intermediates. In the presence of a titanocene catalyst, alkyl Grignard reagents, bromoethanes having a heteroatom at the β-position, and styrene gave regioselectively three-component coupled products (eq. 4).[21] Alkyl radicals generated from the Grignard reagents are considered to add by the aid of the titanocene catalyst across styrene to give benzylic radical intermediates, which are then captured by the alkyl bromides.



While simultaneous formation of two C–C bonds in one-pot is an attractive feature of these multi-component coupling reactions, production of stoichiometric amounts of metal wastes derived from nucleophiles and electrophiles is problematic.

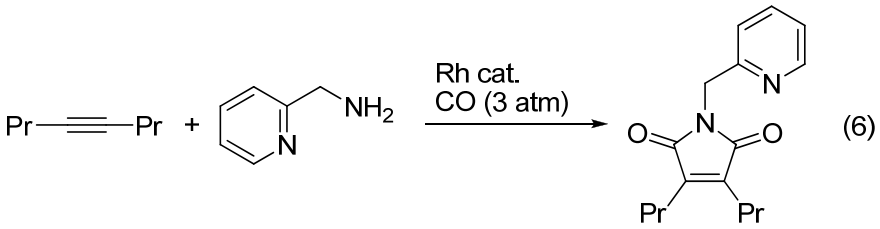
Dicarbonylation of unsaturated bonds

Dicarbonylation of unsaturated C–C bonds is a method to introduce two carbonyls into unsaturated C–C bonds without forming a metal waste. For example, palladium-catalyzed dialkoxycarbonyation of alkynes in an alcoholic solvent under carbon monoxide atmosphere is achieved to give maleic diesters (eq. 5).[22]



(5)

In the presence of pyridin-2-ylmethylamine, maleimide derivatives are obtained by rhodium catalyzed dicarbonylation of alkynes under carbon monoxide atmosphere (eq. 6).[23]

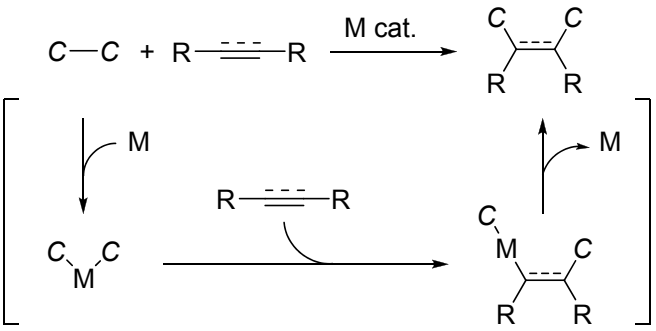


(6)

Although these reactions are useful to functionalize alkynes without byproduct formation, structural diversity of products is apparently limited.

Direct insertion of unsaturated compounds into C–C bonds

Transition metal-catalyzed direct insertion of unsaturated bonds into C–C σ-bonds should be an ultimately ideal transformation in view of atom economy. The catalytic cycle may be involving oxidative addition of a C–C σ-bond to a transition metal catalyst, insertion of an unsaturated bond into the resulting C–M bond, and reductive elimination (Scheme 12). However, the oxidative addition of C–C σ-bonds is not always feasible due to directionally and sterically constrained.[24] Accordingly, successful catalytic processes reported so far have been limited to those involving activation of strained C–C bonds of three- or four-membered compounds.[25,26]



Scheme 12. Possible mechanism for C–C σ-bonds addition across unsaturated C–C bonds.

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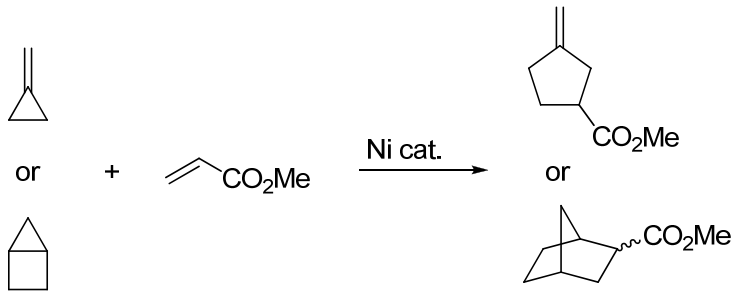
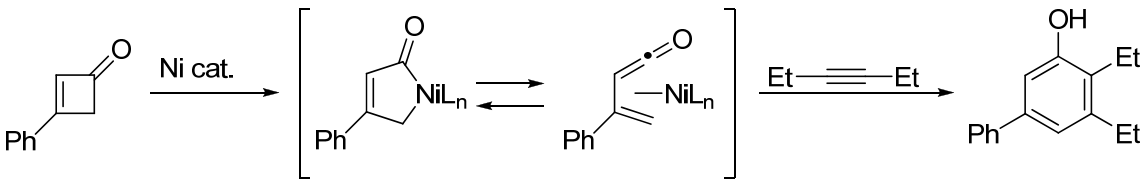
For example, direct insertion of methyl acrylate into the three-membered ring of methylenecyclopropanes and bicyclo[2.1.0]pentanes is catalyzed by a nickel(0) complex to give five-membered ring products (Scheme 13).[25a,b] These reactions are proposed to proceed via oxidative addition of the C–C bond of the cyclopropanes to nickel(0).



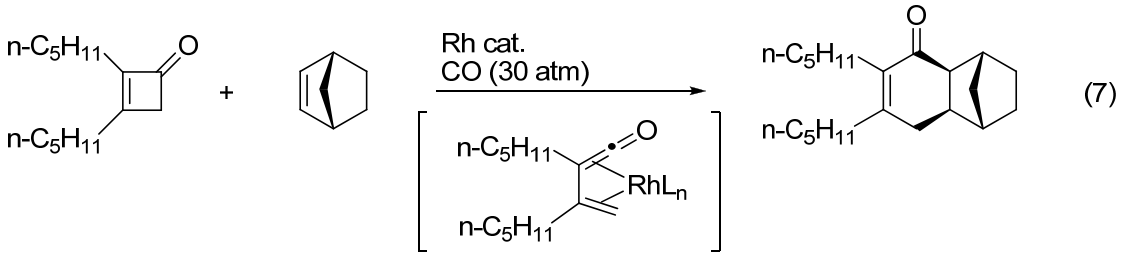
Scheme 13. Nickel-catalyzed direct insertion of cyclopropanes into methyl acrylate.

The C–C bond of cyclobutenones is also activated by nickel and insertion of alkynes n to the C–Ni bond takes place to give phenol derivatives after tautomerization (Scheme 14).[26a]

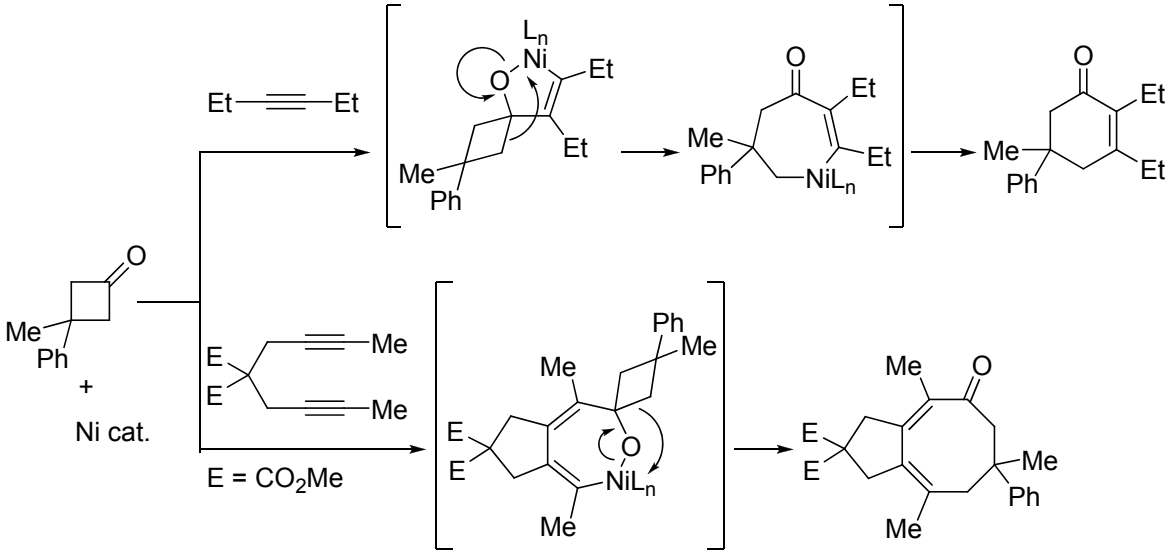


Scheme 14. Nickel-catalyzed direct insertion of alkynes into cyclobutenone.

A similar addition reaction of cyclobutenone across norbornene is catalyzed by rhodium under a carbon monoxide atmosphere (eq. 7).[26e] A catalytic cycle involving a vinylketene–rhodium intermediate has been proposed.

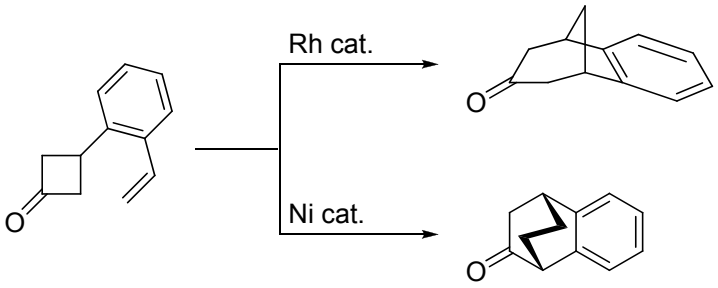


On the other hand, insertion reaction of alkynes into cyclobutanones is catalyzed by nickel. The reaction is proposed to proceed through β-carbon elimination to cleave the C–C bond of oxanickelacycle intermediates.[26f,h] The application of this ring expansion reaction is demonstrated by construction of eight-membered rings using 1,6-diynes (Scheme 15).[26g,j]



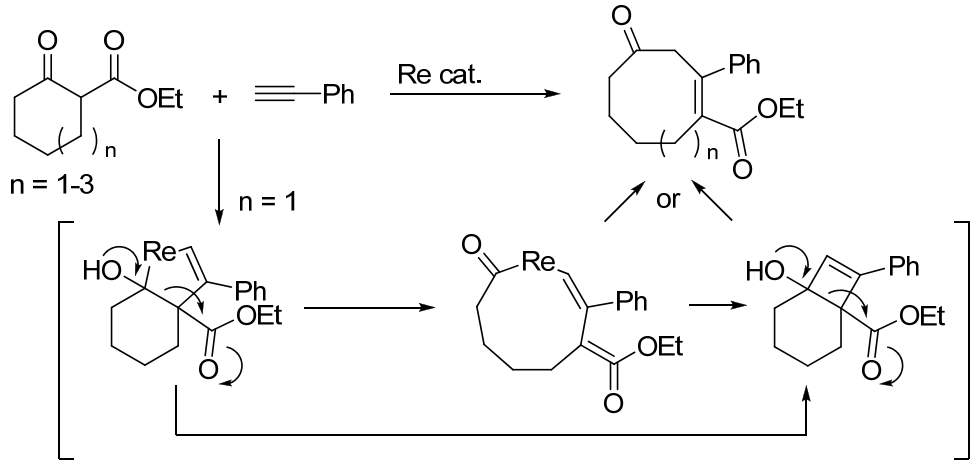
Scheme 15. Nickel-catalyzed cycloaddition of cyclobutanones to alkynes and diynes.

Intramolecular insertion of alkenes into the C–C bond adjacent to carbonyl group of cyclobutanones proceeds in the presence of a rhodium or nickel catalysts.[26b,d,i] The direction of alkene insertion varies depending on the kind of transition metal catalysts (Scheme 16).



Scheme 16. Intramolecular insertion of alkenes into the C–C bond of cyclobutanones.

Cleavage of C–C bonds by retro-aldol-type reactions allows insertion of alkynes into non-strained C–C bonds of β-keto esters with a rhenium catalyst (Scheme 17).[27]



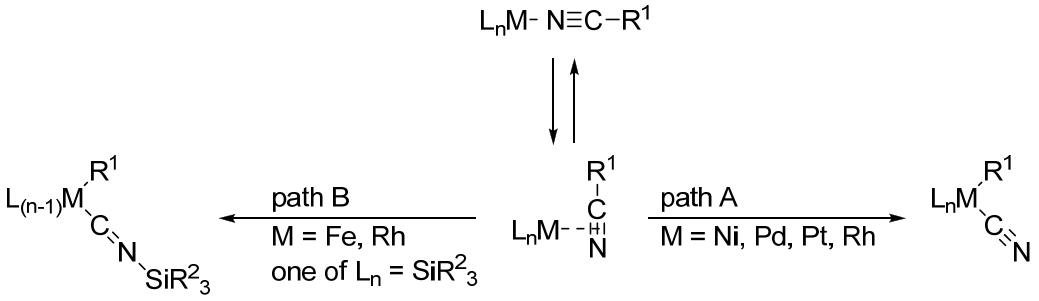
Scheme 17. Rhenium-catalyzed insertion of alkynes into non-strained C–C bonds of β-keto esters.

Apparently, the scope of direct insertion reactions of unsaturated C–C bonds into C–C σ-bonds disclosed so far is severely limited, and, thus, generality and versatility of the transformation remain yet to be explored.

Carbocyanation of unsaturated bonds

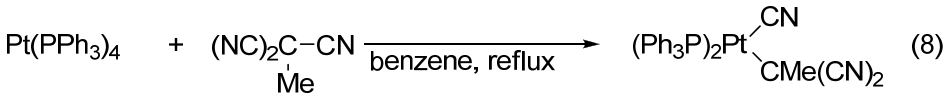
Nitriles are common, ubiquitous in organic chemistry as stable functional molecules. However, C–CN bonds are cleavable upon treatment with certain transition metal complexes, in spite of their high bond dissociation energies (>100 kcal/mol),[28] owing presumably to cyano groups that have good affinity to transition metals and their

strong electron-withdrawing nature in addition to small steric bulk. Nitriles can coordinate to transition metals either in a manner of η^1- or η^2 (Scheme 18).[29] In particular, η^2-coordination further triggers activation of C–CN bonds via oxidative addition (Scheme 18, path A)[30] or formation of silylisonitrile complexes, if a silyl ligand is bound to such metals as rhodium and iron (Scheme 18, path B).[31] A few seminal reports of catalytic reactions utilizing these elemental reactions are available.[32,33]

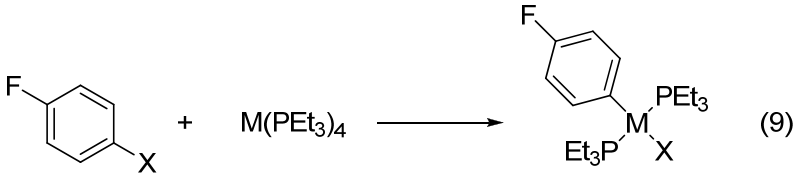


Scheme 18. Activation of C–CN bonds by transition metal complexes.

In 1971, the first example of oxidative addition of C–CN bond was observed in the reaction of 1,1,1-tricyanoethane with $Pt(PPh_3)_4$ in refluxing benzene to afford $Pt(PPh_3)_2(CN)[CMe(CN)_2]$ (eq. 8).[30a]



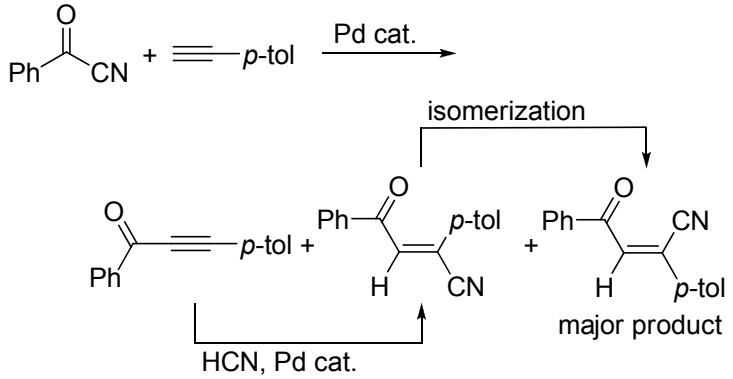
Among the corresponding group 10 transition metal complexes, $Ni(PEt_3)_4$ shows the highest reactivity for oxidative addition of the C–CN bond of 4-fluorobenzonitrile (eq. 9).[30c] The order of the reaction rate with various aryl halides and cyanide is suggested to be I > Br > Cl > CN >> F.



Reactivity
X: **I** > Br > Cl > **CN** >> F
M: **Ni (rt)** > Pd (toluene reflux) > Pt (xylene reflux)

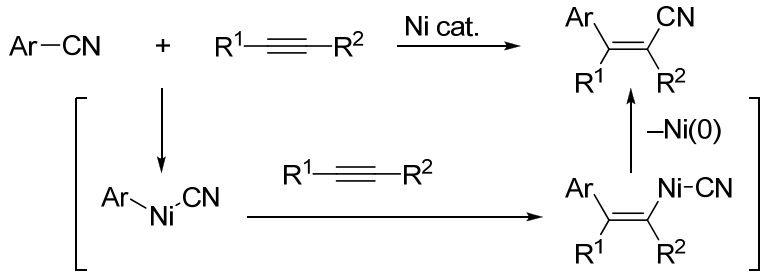
Since the disclosure of these reports, many examples of stoichiometric studies on oxidative additions of C–CN bonds, using especially nickel complexes, have appeared.[30]

An attempt to apply oxidative addition of C–CN bonds to addition reactions was made using benzoyl cyanide and alkynes in the presence of a palladium catalyst.[34] Although this reaction apparently gives expected benzoylcyanation products possibly through oxidative addition of the C–CN bond to palladium(0), the reported reaction pathway involves benzoylation of the terminal alkynes followed by hydrocyanation of the resulting alkynyl ketones, and final isomerization of the double bond. Therefore, the scope of this transformation is applicable only to terminal alkynes (Scheme 19).



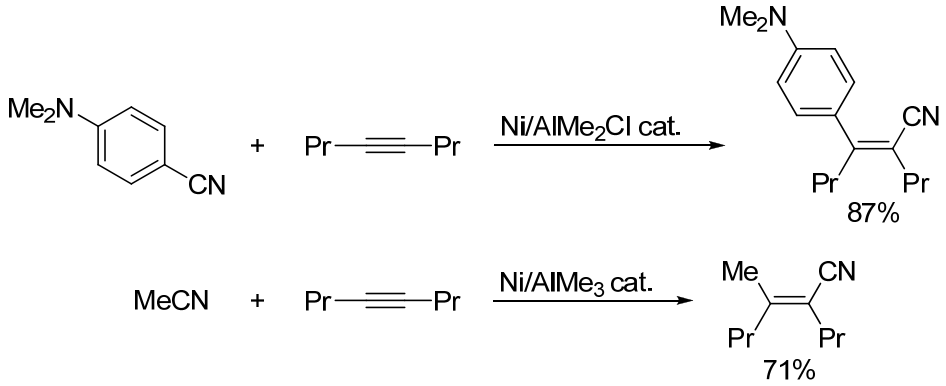
Scheme 19. Palladium-catalyzed benzoylcyanation of terminal alkynes.

In 2004, the nickel-catalyzed addition reaction of aryl cyanides across alkynes was reported.[35] Mechanistically, this was the first demonstration of a true carbocyanation reaction (Scheme 20).



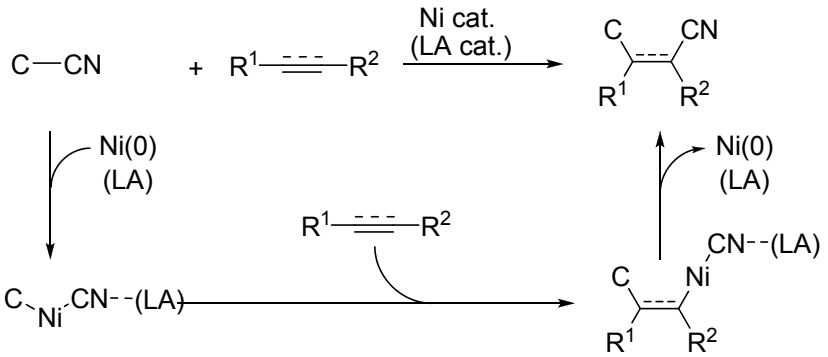
Scheme 20. Nickel-catalyzed arylcyanation of alkynes.

In addition, use of Lewis acid as a cocatalyst was later revealed to dramatically accelerate the arylcyanation reaction.[36] Highly electron-rich aryl cyanides such as 4-aminobenzonitrile, which is inert under the conditions in the absence of a Lewis acid cocatalyst, undergo the reaction in high yields even in the presence of smaller amounts of the nickel catalyst. Furthermore, the nickel/Lewis acid cooperative catalysts allow even acetonitrile to participate in the reaction (Scheme 21).



Scheme 21. Nickel/Lewis acid cocatalysts for carbocyanation of alkynes.

A proposed catalytic cycle involves oxidative addition of C–CN σ-bonds of aryl cyanides to nickel(0). Subsequent coordination and insertion of alkynes followed by reductive elimination give arylcyanation products and regenerate nickel(0) (Scheme 22). All the intermediates as well as transition states of each elemental step have been fully identified by theoretical calculations.[37] In the presence of a Lewis acid cocatalyst, a cyano group should coordinate to the Lewis acid,[38] and then the oxidative addition and/or the reductive elimination[39] are accelerated significantly. Based on this catalytic cycle, a broad scope of both nitriles and unsaturated compounds was established to make the carbocyanation reaction a truly general and useful synthetic tool.

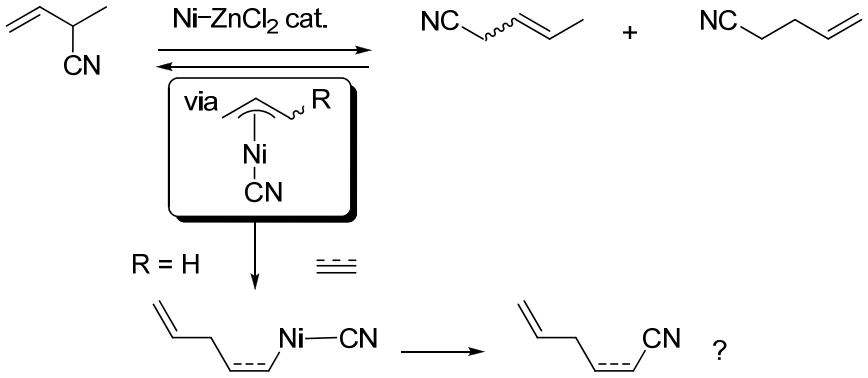


Scheme 22. General mechanism of carbocyanation reactions catalyzed by nickel.

To further expand the scope and generalize the carbocyanation reaction, the author planned to explore the potential of the reaction using other nitriles and unsaturated compounds. He has focused his attention especially on nitriles having functional groups readily convertible to other functionalities.

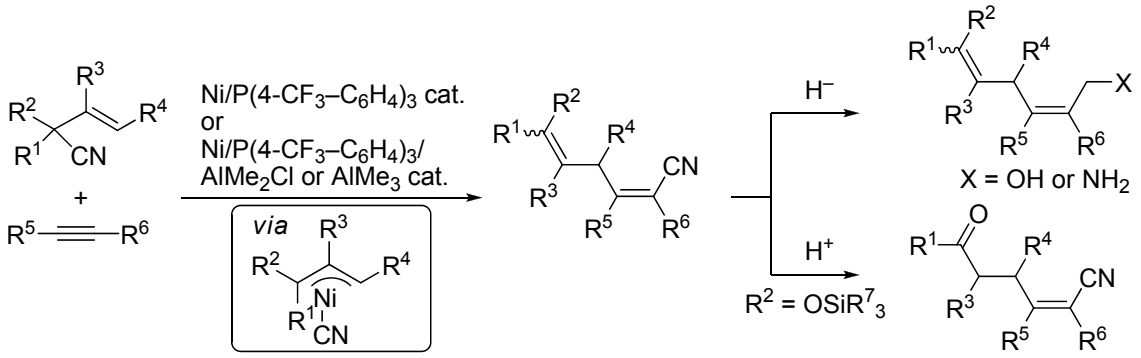
Summary of the present Thesis

It has long been known that the C–CN σ-bond of allyl cyanide oxidatively adds readily to nickel(0) complexes.[40] For example, the DuPont adiponitrile process involves nickel-catalyzed isomerization of 2-methyl-3-pentenenitrile to 3- and 4-pentenenitriles. This reaction proceeds via a π-allylnickel intermediate derived from the oxidative addition of the C–CN σ-bond to nickel(0). Accordingly, he envisaged that insertion of unsaturated compounds into the allyl–Ni bond of the π-allylnickel intermediate followed by reductive elimination could lead to catalytic allylcyanation reaction of unsaturated compounds (Scheme 23).



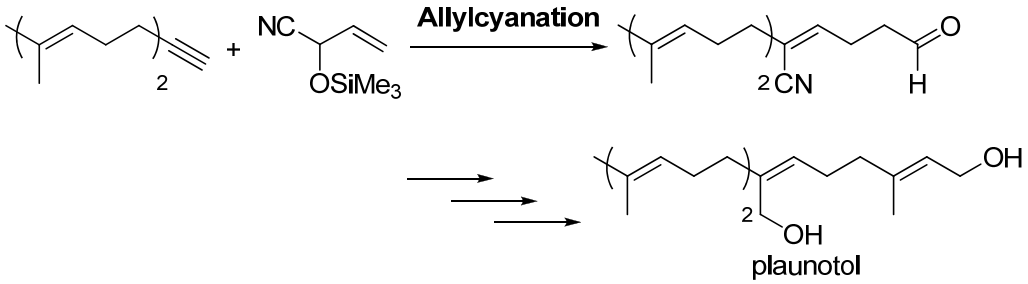
Scheme 23. Nickel-catalyzed isomerization of an allylic nitrile involved in the DuPont adiponitrile process.

In fact, the expected allylcyanation reaction of alkynes proceeds in the presence of a nickel/P(4-CF_3–C_6H_4)$_3$ catalyst exclusively in a *cis*-fashion as described in Chapter 2 (Scheme 24).[41] α-Siloxyallyl cyanides also add across alkynes at the γ-position. Lewis acid catalyst work extremely well to reduce catalyst loadings and the amount of allyl cyanides, allowing an equimolar reaction and also expansion of the substrate scope.



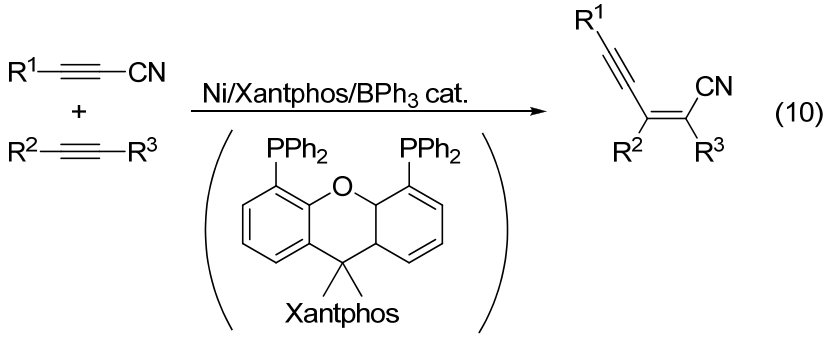
Scheme 24. Nickel or nickel/Lewis acid-catalyzed allylcyanation of alkynes.

The allylcyanation reaction allows simultaneous installation of a cyano group and a linear C_3 functional unit, serving thereby as a key step in the stereoselective concise synthesis of plaunotol, a drug for treatment of gastric ulcer (Scheme 25).[42,43]

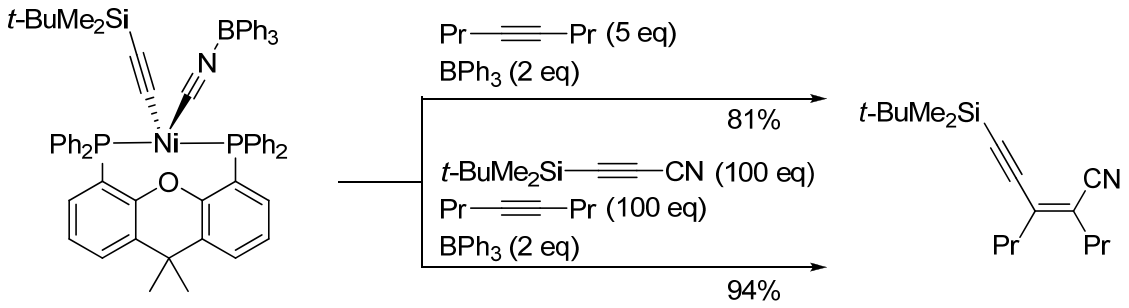


Scheme 25. Concise synthesis of plaunotol using allycyanation reaction as a key step.

Alkynylcyanation of alkynes and dienes[44] is described in Chapter 3. A nickel/Xantphos/BPh_3 catalyst is found effective for the activation of the C(sp)–CN σ-bonds of alkynyl cyanides and *cis*-addition reaction across alkynes to give conjugated enynenitriles (eq. 10).

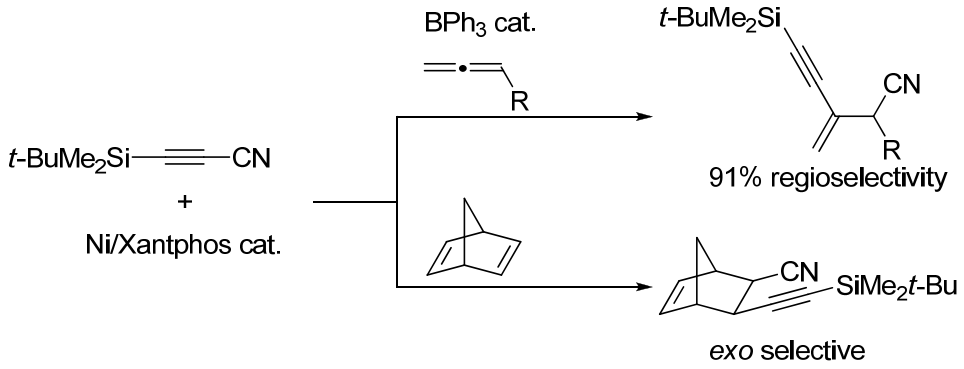


A mechanistic scheme initiated by oxidative addition of alkynyl cyanides to nickel(0) has been proposed and identified by structural characterization of the oxidative adduct and its stoichiometric and catalytic reactions with alkynes to afford the corresponding alkynylcyanation product (Scheme 26).



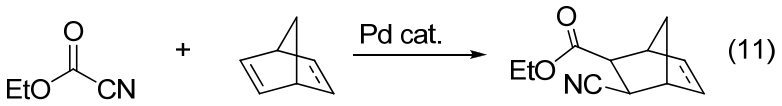
Scheme 26. Reactions of *trans*-(xantphos)Ni(CNBPh$_3$)(C≡CSiMe$_2$*t*-Bu), a plausible intermediate of alkynylcyanation of alkynes.

Alkynyl cyanides were also found to add across 1,2-dienes and norbornadiene in the presence of nickel/Xantphos/BPh$_3$ or nickel/Xantphos catalyst with high regio- and stereoselectivity, respectively (Scheme 27).



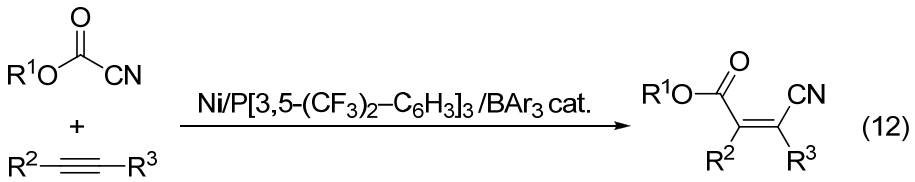
Scheme 27. Alkynylcyanation of 1,2-dienes and norbornadiene catalyzed by nickel

Chapter 4 describes cyanoesterification of unsaturated bonds which allows introduction of both alkoxycarbonyl and cyano groups into alkenes and alkynes simultaneously in a stereospecific manner. The functional groups thus introduced can be transformed independently by their rich chemistry. Although the same transformation was reported using palladium catalysts, the scope of unsaturated compounds is severely limited to norbornene and norbornadiene (eq. 11).[45]



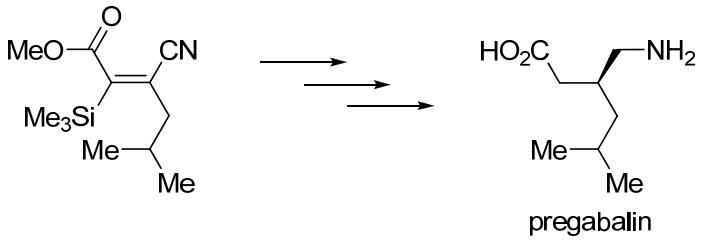
(11)

The author has demonstrated that the nickel catalysis is far more versatile for the cyanoesterification reaction of various unsaturated compounds. For example, nickel/BAr_3 catalysts allow regio- and stereoselective cyanoesterification of alkynes to give highly functionalized alkenenitriles (eq. 12).[46]



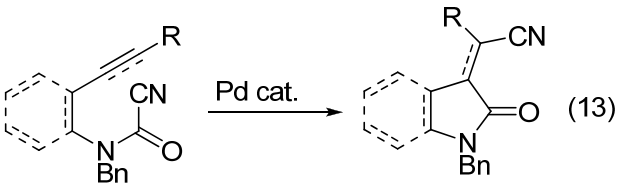
(12)

The cyano group of the resulting adducts can be reduced with the ester group intact as demonstrated by a formal synthesis of pregabalin,[47,48] an anticonvulsant drug used for treatment of neuropathic pain (Scheme 28).



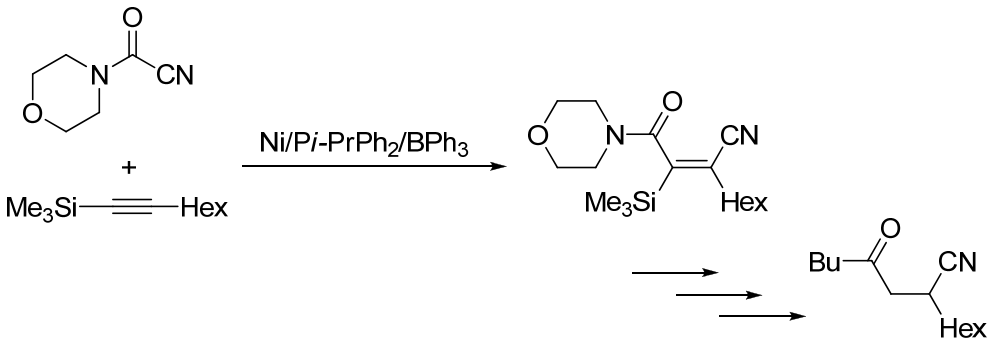
Scheme 28. Alkyne cyanoesterification as appplied to formal synthesis of pregabalin.

Carbamoyl cyanides are also attractive nitrile substrates for the carbocyanation reaction. Palladium-catalyzed cyanocarbamoylation reactions of alkynes, alkenes, and 1,2-dienes are reportedly limited to intramolecular variants (eq. 13).[49]



(13)

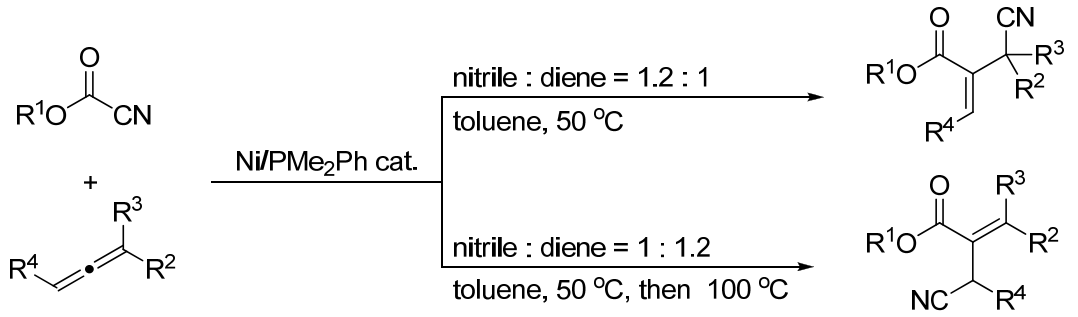
Regio- and stereoselective intermolecular cyanocarbamoylation of alkynes has been achieved by the nickel/BPh_3 catalyst. The adduct having a morpholinamide can be transformed to a β-cyano ketone by chemoselective transformations of the amide and alkenyl groups (Scheme 29).



Scheme 29. Intermolecular cyanocarbamoylation of alkynes catalyzed by nickel/BAr_3.

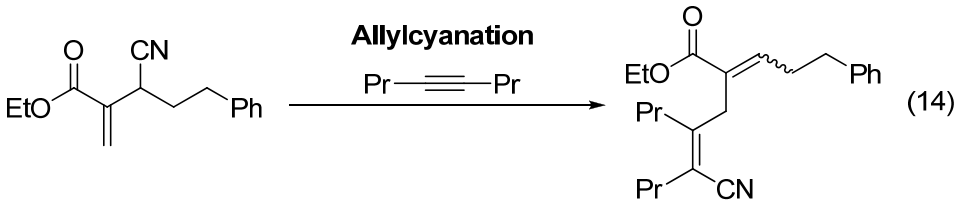
Attempted addition reactions of cyanoformate of pentanethiol and benzoyl cyanide across alkynes are also discussed briefly in this Chapter.

Demonstrated in Chapter 5 is regio- and stereoselective cyanoesterification of 1,2-dienes to give highly functionalized β-cyano-α-methylenealkanoates.[50] By simply changing molar ratios of reactants and reaction temperature, the regioselectivity of the cyanoesterification can be controlled (Scheme 30). Mechanistic details including explanation for the regiodiversity are also discussed.



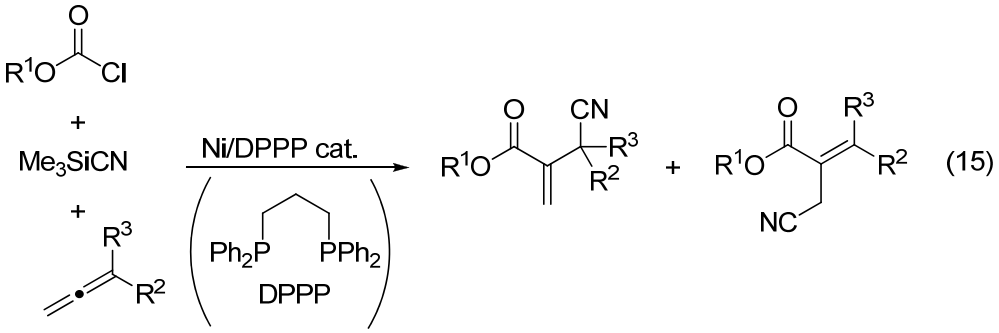
Scheme 30. Cyanoesterification of 1,2-diene catalyzed by nickel.

Further synthetic elaboration to form C–C σ-bonds using the cyanoesterification products is demonstrated by allylcyanation reaction across alkynes to attain three-component coupling based on nickel catalysis (eq. 14).[41]



(14)

In view that cyanoformate esters are generally prepared from the corresponding chloroformate esters and metal cyanides,[51] nickel-catalyzed cyanoesterification of 1,2-dienes has been examined using silyl cyanides, chloroformates, and 1,2-dienes. The three-component coupling should be a straightforward protocol to introduce various alkoxycarbonyl and cyano groups without the preparation of cyanoformate esters as demonstrated in Chapter 5 (eq. 15).



(15)

In summary, the present Thesis demonstrates that novel nickel-catalyzed carbocyanation reactions of unsaturated compounds producing highly functionalized

nitriles, which are otherwise difficult to obtain. The transformations represent a new class of difunctionalization reactions of unsaturated bonds without forming any byproducts. Because a wide variety of starting nitriles are readily available, carbocyanation is much more versatile than related transformations reported previously. In addition, rich chemistry of the cyano group should definitely make the present novel transformation highly attractive and will find wide applications in organic synthesis.

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Chapter 2

Allylcyanation of Alkynes Catalyzed by Nickel

Allyl cyanides are found to add across alkynes in the presence of a nickel/P(4-CF_3–C_6H_4)$_3$ catalyst to give stereo- and regiochemically defined substituted 2,5-hexadienenitriles. Use of $AlMe_2Cl$ or $AlMe_3$ as a Lewis acid cocatalyst has been found to significantly accelerate the reaction and expand the substrate scope. The cyano group in the allylcyanation products can be transformed to a hydroxymethyl or aminomethyl group to afford highly substituted allylic alcohols or amines. α-Siloxyallyl cyanides also add across alkynes selectively at the less hindered γ-carbon to allow introduction of 3-oxo-propyl functionality after hydrolysis of the resulting sily enol ethers. This particular allylcyanation reaction has been employed for the stereoselective construction of the tri-substituted double bond of plaunotol, an antibacterial natural product active against *Helicobacter pylori*.

Introduction

Development of regio- and stereoselective construction of poly-substituted ethenes is an important issue in synthetic organic chemistry.[1] Of many synthetic methods, transition metal-catalyzed regio- and stereoselective addition reactions across alkynes have been advanced significantly to be particularly useful protocols. For example, allylfunctionalization reactions such as allylmetalation,[2] allylhalogenation,[3] and allylchalcogenation[4] and subsequent C–C bond forming reactions are powerful and straightforward methods to access synthetically versatile highly substituted 1,4-diene structures. Ultimately, however, direct insertion of alkynes into an allylic C–C bond should be of great synthetic potential to construct such structures efficiently. On the other hand, carbocyanation reactions of alkynes have appeared recently as new efficient methods for stereo- and regioselective construction of poly-substituted ethenes.[5,6] While various nitriles have been demonstrated to participate in the carbocyanation reaction through oxidative addition of C–CN bonds to palladium(0) or nickel(0), allyl cyanides have been expected to be a promising substrate for the transformation because their C–CN bonds have also been known to undergo the oxidative addition readily to nickel(0).[7] A representative example is seen in the DuPont adiponitrile process, which utilizes nickel-catalyzed isomerization of 2-methyl-3-pentenenitrile to 3- and 4-pentenenitriles through oxidative addition of the C–CN bond to nickel(0).[8] A resulting π-allylnickel intermediate is suggested to undergo reductive elimination at the less hindered carbon to give linear 3-pentenenitrile, which further hydrocyanated to give finally adiponitrile. Accordingly, the author envisaged that insertion of alkynes into the allyl–Ni bond of the π-allyl nickel intermediate[9] followed by reductive elimination could lead to catalytic allylcyanation reaction of alkynes. Herein described is nickel- or nickel/Lewis acid-catalyzed regio- and stereoselective allylcyanation of alkynes to afford highly functionalized poly-substituted acrylonitriles with variety of functional groups.[10] He also demonstrates the synthetic utility of the allylcyanation reaction by efficient synthesis of the tri-substituted ethene moiety of plaunotol, an antibacterial particularly effective against *Helicobacter pylori*.

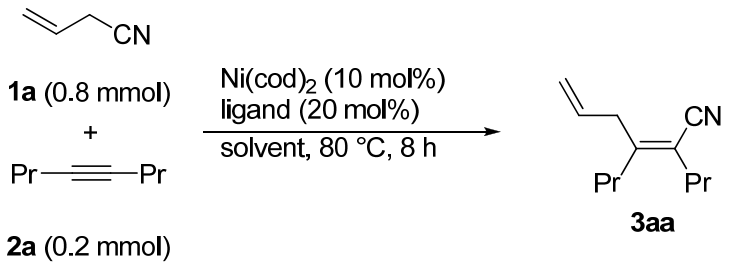
Results and discussion

Nickel-catalyzed allylcyanation of alkynes

The author first examined the reaction of allyl cyanide (**1a**, 4.0 mmol) with 4-octyne (**2a**, 1.0 mmol) in acetonitrile at 80 °C in the presence of $Ni(cod)_2$ (10 mol%) and various phosphine ligands (Table 1). Of ligands examined, $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (20 mol%) was found to be the most effective to give (*Z*)-2,3-dipropylhexa-2,5-dienenitrile (**3aa**) in 78% yield after isolation (entry 1). The stereochemistry was unambiguously assigned by nOe experiments irradiating the allylic methylenes in ^1H NMR analyses. An equimolar reaction resulted in low yield due presumably to formation of unidentified side products derived from side reactions of allyl cyanide (entry 2). Phosphorus ligands having electron-donating substituents, and phosphites and less polar solvents all retarded the reaction (entries 3–9).

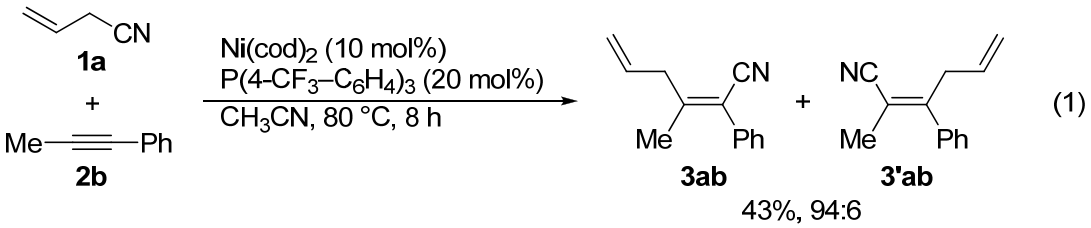
With the optimized conditions in hand, the author next examined the scope of the reaction (Table 2 and eq. 1). The carbocyanation of **2a** with both 3-pentenenitrile (**1b**) and 2-methyl-3-butenenitrile (**1c**) gave the same crotylcyanation product **3ba** as a mixture of stereoisomers in similar yields with similar stereoselectivity (entries 1 and 2). No trace amount of an α-adduct was obtained with **1c**, suggesting a catalytic cycle involving a π-crotylnickel intermediate. The reactions of (*E*)-5,5-dimethyl-3-hexenenitrile (**1d**) and (*E*)-4-phenyl-3-butenenitrile (**1e**) gave the corresponding adducts as single stereoisomers possibly through a *syn*-π-allylnickel species (entries 3 and 4). The addition of cyclopenten-1-ylacetonitrile (**1f**) turned out to be sluggish (entry 5). The addition of **1a** across 1-phenyl-1-propyne (**2b**) gave a mixture of two regioisomers (**3ab**/**3'ab** = 94 : 6) in 43% yield (eq. 1). An isomer having a phenyl group at the cyano-substituted carbon was obtained as a major product. The regiochemistry was unambiguously assigned by ^1H NMR nOe experiments. On the other hand, reactions with terminal alkynes such as 1-octyne gave no detectable amount of allycyanation products due to rapid trimerization and/or oligomerization of the alkynes.

Table 1. Nickel-catalyzed allylcyanation of 4-octyne (**2a**).[a]



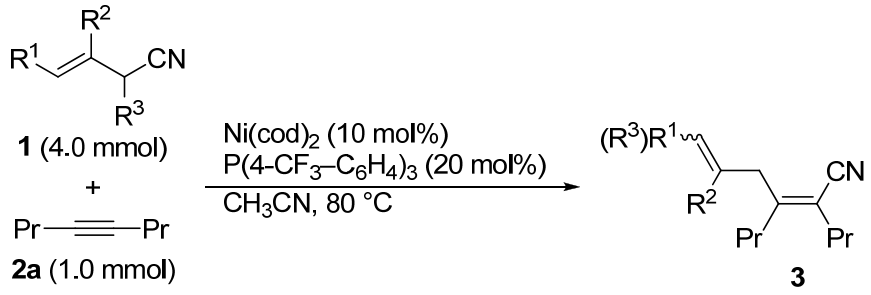
Entry	Ligand	Solvent	Yield of **3aa** (%)[b]
1[c]	$P(4\text{-}CF_3\text{–}C_6H_4)_3$	CH_3CN	98 (78)[d]
2[e]	$P(4\text{-}CF_3\text{–}C_6H_4)_3$	CH_3CN	35
3	$P(4\text{-}CF_3\text{–}C_6H_4)_3$	DMF	70
4	$P(4\text{-}CF_3\text{–}C_6H_4)_3$	1,4-dioxane	39
5	$P(4\text{-}CF_3\text{–}C_6H_4)_3$	toluene	22
6	PPh_3	CH_3CN	61
7	$P(4\text{-}MeO\text{–}C_6H_4)_3$	CH_3CN	8
8	PMe_3	CH_3CN	0
9	$P(OPh)_3$	CH_3CN	2

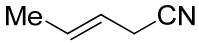
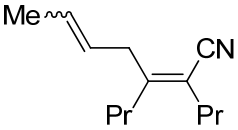
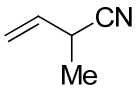
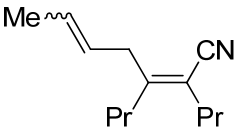
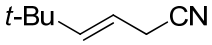
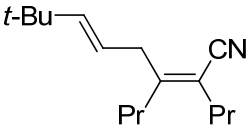
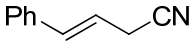
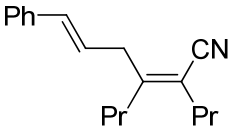
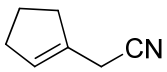
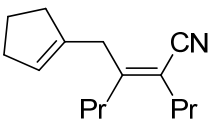
[a] All the reaction was carried out using **1a** (0.80 mmol), **2a** (0.20 mmol), $Ni(cod)_2$ (20 μmol), and ligand (40 μmol) in a solvent (0.40 mL) at 80 °C for 8 h. [b] Estimated by GC using $C_{14}H_{30}$ as an internal standard. [c] The reaction was carried out using **1a** (4.0 mmol) and **2a** (1.00 mmol). [d] Isolated yield based on **2a**. [e] The reaction was carried out using **1a** (0.20 mmol) and **2a** (0.20 mmol).



(1)

Table 2. Allylcyanation of 4-octyne (**2a**) using substituted allyl cyanides catalyzed by nickel.[a]



Entry	**1**	Time (h)	Product(s)	Yield (%)[b] (*5E*:*5Z*)[c]
1	 **1b**	17	 **3ba**	69 (85:15)
2	 **1c**	17	 **3ba**	55 (83:17)
3	 **1d**	18	 **3da**	49 (>99:1)
4[d]	 **1e**	18	 **3ea**	86 (>99:1)
5	 **1f**	106	 **3fa**	21

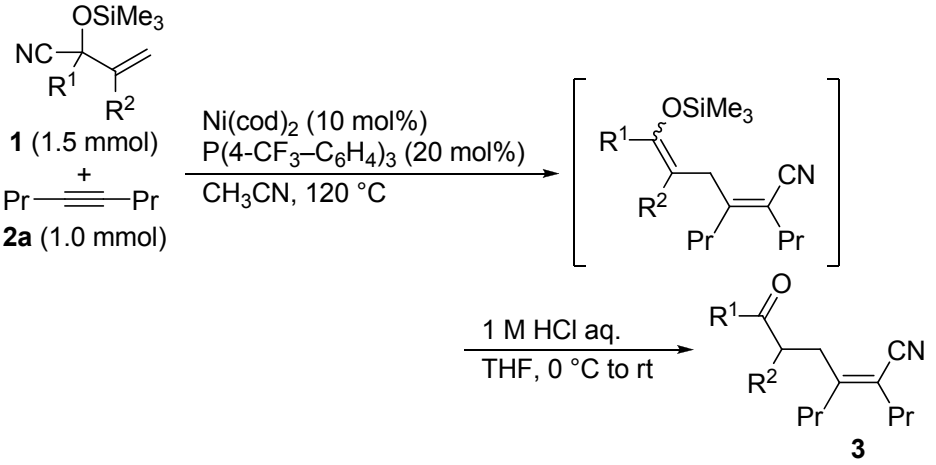
[a] All the reaction was carried out using a nitrile (4.0 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.20 mmol) in CH_3CN (2.0 mL) at 80 °C. [b] Isolated yields based on **2a**. [c] Estimated by ^1H NMR and/or GC analysis of a crude and/or purified product. [d] The reaction was carried out in CH_3CN (1.00 mL).

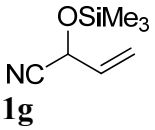
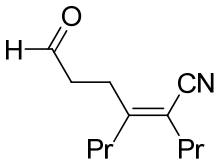
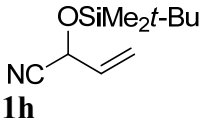
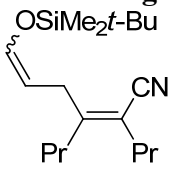
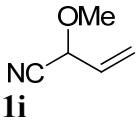
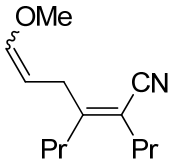
Nickel-catalyzed carbocyanation of alkynes using α-siloxyallyl cyanides

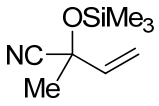
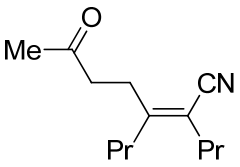
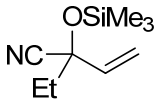
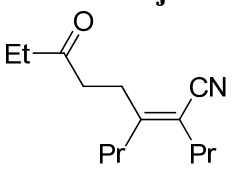
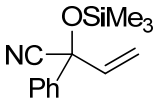
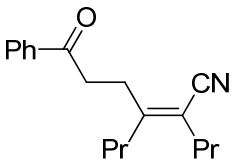
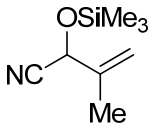
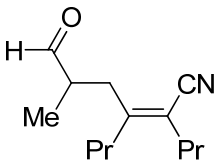
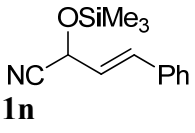
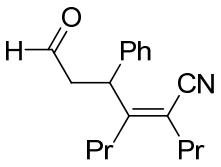
α-Siloxyallyl cyanide (**1g**), readily available from acrolein and trimethylsilyl cyanide, also underwent the carbocyanation reaction (Table 3).[11] Worth to note is that **1g** (1.5 mmol) reacted with **2a** exclusively at the γ-carbon of **1g** to give aldehyde **3ga** in

81% yield after hydrolysis of the resulting silyl enol ether (entry 1). Reaction of *α*-*tert*-butyldimethylsiloxyallyl cyanide (**1h**) and *α*-methoxyallyl cyanide (**1i**) gave the corresponding enol ether products, which were successfully isolated by silica gel column chromatography as a mixture of stereoisomers (entries 2 and 3). Silyl ethers of enone cyanohydrins also reacted similarly at 120 °C to give the corresponding cyanoketones (entries 4–6). Whereas a *β*-substituent in **1m** did not affect the reaction to give aldehyde **3ma** in good yield at 80 °C (entry 7), *γ*-substituted *α*-siloxyally cyanide **1n** did not participate in the reaction (entry 8).

Table 3. Carbocyanation of 4-octyne (**2a**) using *α*-siloxyallyl cyanides catalyzed by nickel.[a]



Entry	**1**	Time (h)	Product	Yield (%)[b] (*5E*:*5Z*)[c]
1[d]	 **1g**	1	 **3ga**	81
2[d]	 **1h**	5	 **3ha**	87 (52:48)
3[d]	 **1i**	5	 **3ia**	82 (22:78)

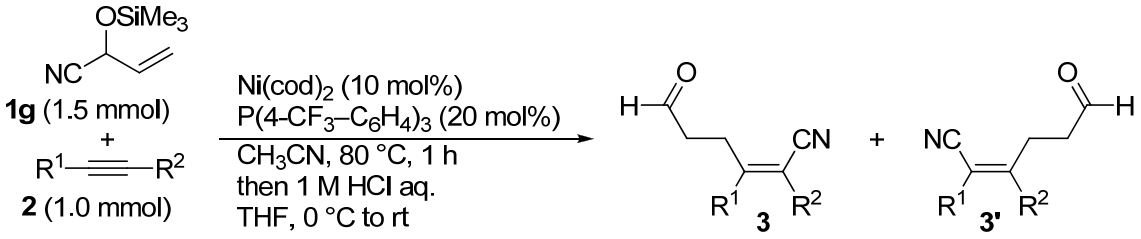
4	 **1j**	2	 **3ja**	79
5	 **1k**	3	 **3ka**	81
6	 **1l**	2	 **3la**	54
7[d]	 **1m**	12	 **3ma**	69
8	 **1n**	12	 **3la**	<5

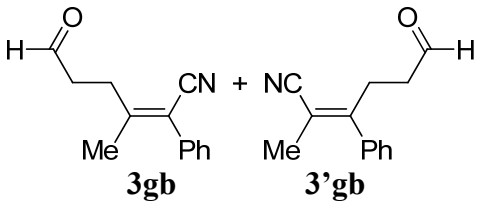
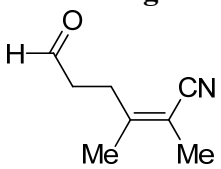
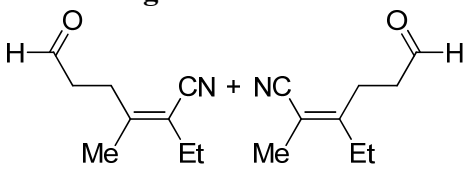
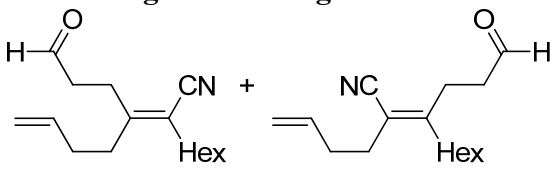
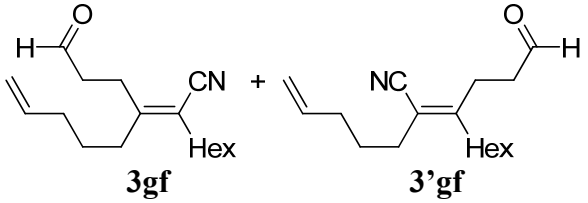
[a] All the reaction was carried out using a nitrile (1.50 mmol), **2a** (2.0 mmol), $Ni(cod)_2$ (0.100 mmol), and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.20 mmol) in CH_3CN (1.00 mL) at 120 °C, and crude products were treated with 1 M HCl aq. in THF at 0 °C to rt. [b] Isolated yields based on **2a**. [c] Estimated by ^1H NMR analysis of a crude and/or purified product. [d] The reactions were carried out in toluene at 80 °C.

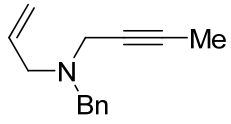
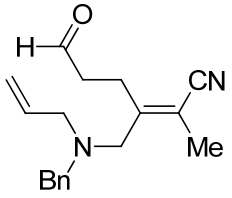
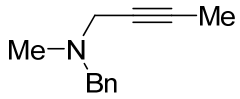
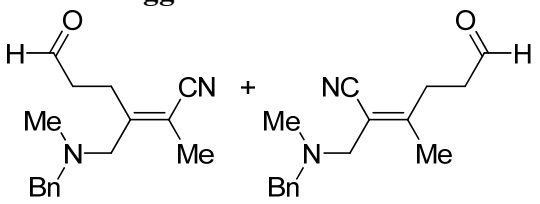
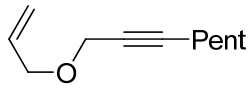
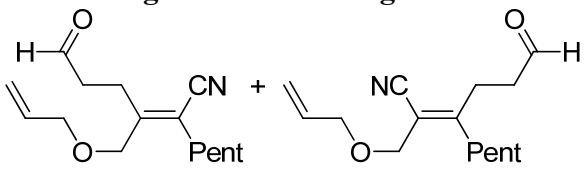
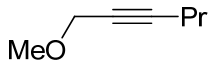
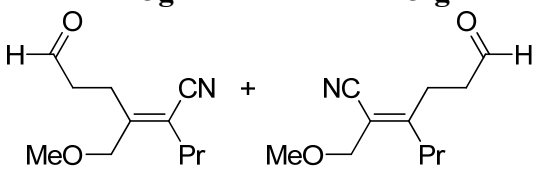
Various internal alkynes were examined next for the reaction with **1g** (Table 4). Addition of **1g** across **2b** proceeded in good yield with high regioselectivity (entry 1). The moderate yield of **3gc** was obtained with 2-butyne (**2c**) due presumably to its higher rate of competitive trimerization and/or oligomerization under the reaction conditions (entry 2). Poor or no regioselection was observed with alkynes having sterically similar substituents **2d**–**2f** (entries 3–5).[12] Alternatively, heteroatoms such as oxygen and nitrogen at a propargylic position of alkynes were found to effect regioselection of the carbocyanation (entries 6–9). It is remarkable that the effect was further intensified by introducing an allyl group on the propargylic heteroatoms (entry 6 vs. entry 7 and entry

8 vs. entry 9).

Table 4. Carbocyanation of internal alkynes using **1g** catalyzed by nickel.[a]



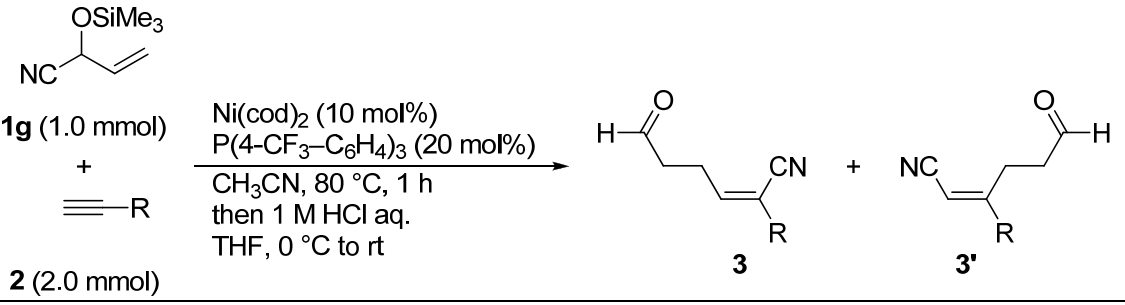
Entry	**2**	Product(s)	Yield (%)[b] (**3**:**3'**)[c]
1	Me—≡—Ph **2b**	 **3gb** **3'gb**	70 (93:7)
2	Me—≡—Me **2c**	 **3gc**	58
3	Me—≡—Et **2d**	 **3gd** **3'gd**	58 (61:39)
4	≡—Hex **2e**	 **3ge** **3'ge**	69 (50:50)
5	≡—Hex **2f**	 **3gf** **3'gf**	51 (50:50)

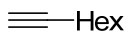
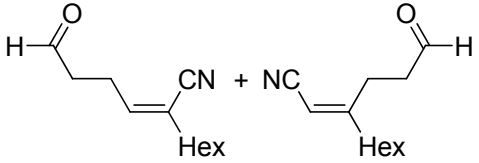
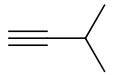
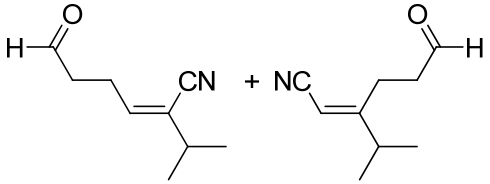
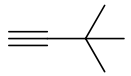
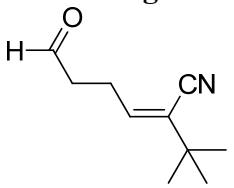
6	 **2g**	 **3gg**	48 (>95:5)
7	 **2h**	 **3gh** + **3'gh**	51 (73:27)
8	 **2i**	 **3gi** + **3'gi**	57 (94:6)
9	 **2j**	 **3gj** + **3'gj**	66 (83:17)

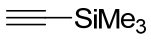
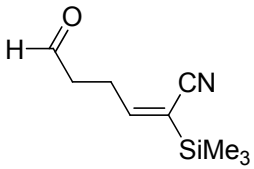
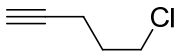
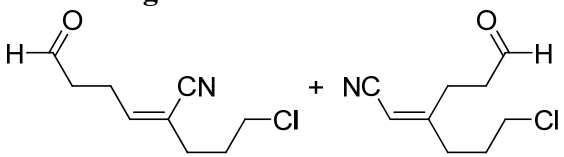
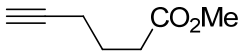
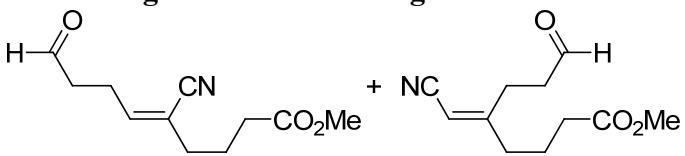
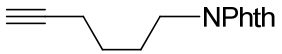
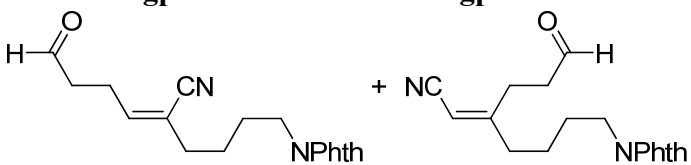
[a] All the reaction was carried out using **1g** (1.50 mmol), an alkyne (2.0 mmol), $Ni(cod)_2$ (0.100 mmol), and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.20 mmol) in CH_3CN (1.0 mL) at 80 °C for 1 h, and crude products were treated with 1 M HCl aq. in THF at 0 °C to rt. [b] Isolated yields of an inseparable mixture of two regioisomers based on **2**. [c] Determined by ^1H NMR and/or GC analysis of a crude and/or purified product.

The author further found that **1g** underwent the carbocyanation reaction across terminal alkynes in modest to good yields (Table 5). To push the reaction effectively as compared with cyclotrimerization and/or oligomerization of alkynes, use of two molar equivalents of terminal alkynes is preferred. The reactions were smooth and regioselective like the ones with internal alkynes: adducts having a substituent at a cyano-substituted carbon were major products. The reaction tolerated a gram-scale synthesis (entry 1). Excellent regioselectivity was observed with alkynes having a bulky substituent such as *t*-Bu and $SiMe_3$ (entries 3 and 4). Terminal alkynes having various functional groups including chloro, ester, and *N*-phthalimidoyl underwent the reaction to give the corresponding functionalized allylcyanation products in good yields (entries 5–7).

Table 5. Allylcyanation of terminal alkynes using **1g** catalyzed by nickel.[a]



Entry	Alkyne (**2**)	Product(s)	Yield (%),[b] (**3**:**3'**)[c]
1[d]	 **2k**	 **3gk** **3'gk**	74 (92:8)
2	 **2l**	 **3gl** **3'gl**	48 (95:5)
3	 **2m**	 **3gm**	61 (>99:1)

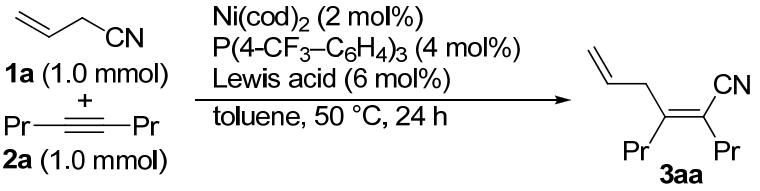
4	 **2n**	 **3gn**	36 (>99:1)
5	 **2o**	 **3go** **3'go**	78 (95:5)
6	 **2p**	 **3gp** **3'gp**	62 (95:5)
7	 **2q**	 **3gq** **3'gq**	60 (90:10)

[a] All the reaction was carried out using **1g** (1.00 mmol), an alkyne (2.0 mmol), $Ni(cod)_2$ (0.100 mmol), and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.20 mmol) in CH_3CN (1.0 mL) at 80 °C for 1 h, and crude products were treated with 1 M HCl aq. in THF at 0 °C to rt. [b] Isolated yields of an inseparable mixture of two regioisomers based on **1g**. [c] Determined by ^1H NMR and/or GC analysis of a crude and/or purified product. [d] The reaction was carried out using **1g** (15 mmol) and **2k** (30 mmol).

Allylcyanation of alkynes catalyzed by nickel/Lewis acid

It has recently been reported that the arylcyanation of alkynes is significantly accelerated by a Lewis acid cocatalyst.[6c] The effect of BPh_3 as a Lewis acid on the oxidative addition of allyl cyanides to a nickel(0)/bisphosphine complex has also been revealed in detail by Jones making the elemental reaction preferable kinetically and thermodynamically compared with competitive oxidative addition of the allylic C–H bond.[7c] Because unidentified side reactions of allyl cyanide **1a** could be ascribed to this competitive pathway and, thus, use of **1a** in excess was essential to obtain allylcyanation products in good yields, the author anticipated use of a Lewis acid cocatalyst would be beneficial for the allylcyanation reaction especially with **1a**. Of Lewis acid cocatalysts examined for the reaction of **1a** with **2a**, $AlMe_2Cl$ (6 mol%) was found to be the most effective to give **3aa** in 96% yield even using allyl cyanide (**1a**) and 4-octyne (**2a**) in stoichiometric amounts and the same nickel catalyst with a decreased amount (2 mol%) in toluene at 50 °C (entry 2 of Table 6). $AlMe_3$, $AlMeCl_2$, and BPh_3 were not as effective as $AlMe_2Cl$ (entries 1, 3, and 4), whereas the absence of Lewis acid gave only a trace amount of **3aa** under the modified conditions (entry 5). Use of polar solvents such as acetonitrile, 1,4-dioxane, and DMF was futile.

Table 6. Effect of Lewis acid cocatalysts on the reaction of **1a** with **2a**.[a]

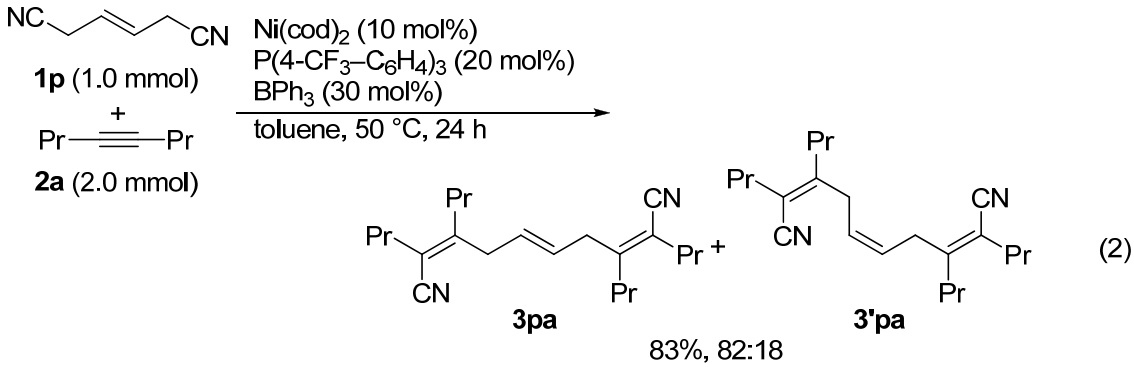


Entry	Lewis acid	Yield (%)[b]
1	$AlMe_3$	6
2	$AlMe_2Cl$	96[c]
3	$AlMeCl_2$	51
4	BPh_3	39
5	none	2

[a] All the reaction was carried out using **1a** (1.00 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (20 μmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (40 μmol), and Lewis acid (60 μmol) in toluene (1.00 mL) at 50 °C for 24 h. [b] Determined by GC using $C_{14}H_{30}$ as an internal standard. [c] Isolated yield.

With the nickel/$AlMe_2Cl$ catalyst in hand, the author reexamined the scope of the allylcyanation reaction (Table 7). Substituted allyl cyanides **1e** and **1f** underwent the equimolar reaction with **2a** with 2 mol% of the nickel catalyst at 50 °C (entries 1 and 2). γ,γ-Di-substituted allyl cyanide such as prenyl cyanide (**1o**), which is inert under the conditions in the absence of a Lewis acid cocatalyst, undergo the reaction in moderate yield (entry 3). The scope of alkynes with **1a** a nitrile substrate was significantly expanded to include various terminal alkynes (entries 4–9). Complete regioselectivity observed with the terminal alkynes is particularly useful from a synthetic viewpoint (entries 5–9). Highly substituted allylsilane **3ar** was obtained from propargylsilane **2r** albeit in a modest yield (entry 6). Functional groups such as chloro, cyano, and siloxy did not affect the Lewis acid cocatalysis (entries 7–9).

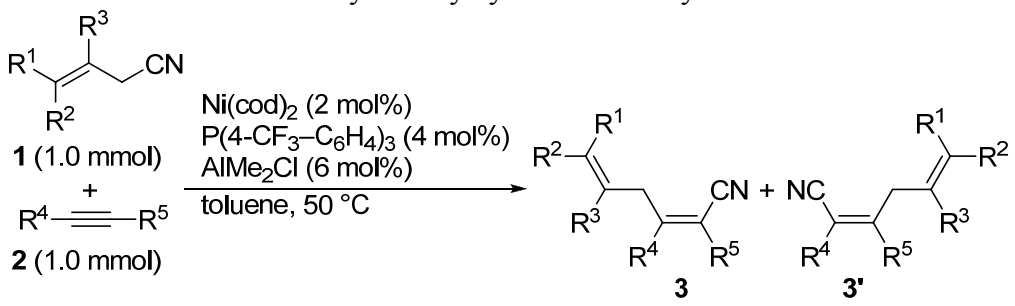
The reaction of **1p** having two allylic cyanide moieties with two molar equivalents of **2a** and BPh_3 as a Lewis acid cocatalyst gave double allylcyanation products **3pa** and **3'pa** (eq. 2). Isomerization of the double bond in **1p** was observed to be responsible for the formation of **3'pa**.

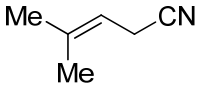
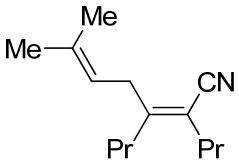
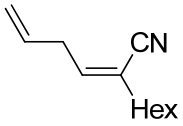
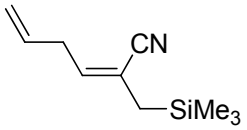
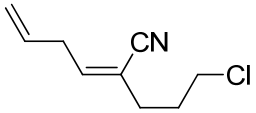
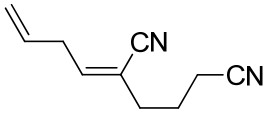
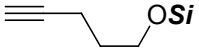
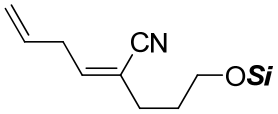


(2)

The binary catalysis was found also effective for the carbocyanation reaction using α-siloxyallyl cyanide (**1g**). The reaction of **1g** (1.00 mmol) with **2a** (1.00 mmol) in the presence of $Ni(cod)_2$ (2 mol%), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (4 mol%), and $AlMe_3$ (8 mol%) in toluene at 50 °C for 12 h gave **3ga** in 80% yield after acidic hydrolysis of the resulting silyl enol ether (entry 1). Variously functionalized di-substituted acrylonitriles were obtained with excellent stero- and regioselectivities (entries 2–6). In these reactions, $AlMe_2Cl$ was less effective.

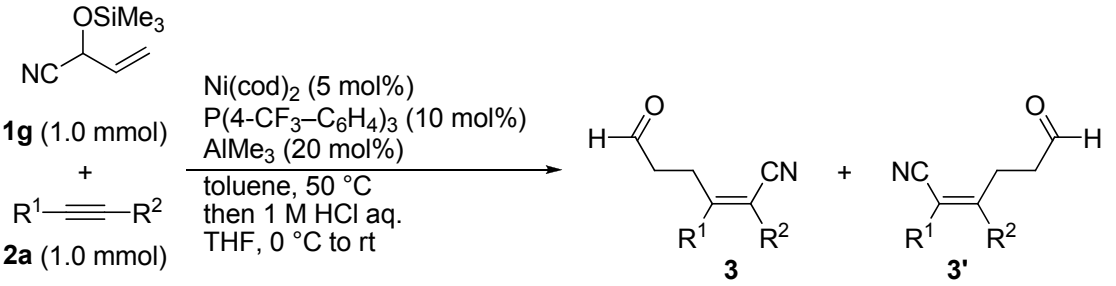
Table 7. Nickel/Lewis acid-catalyzed allylcyanation of alkynes.[a]

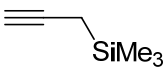
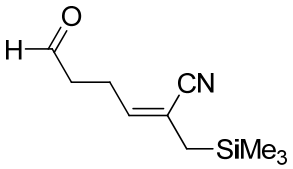
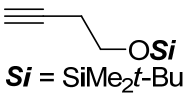
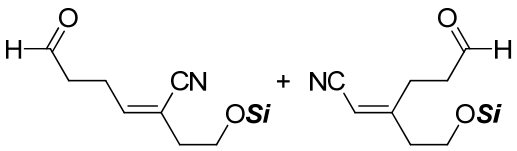


Entry	**1**	**2**	Time (h)	Product(s)	Yield (%)[b] (**3**:**3'**)[c]
1	**1e**	**2a**	72	**3ea**	74
2	**1f**	**2a**	48	**3fa**	82
3[d]	 **1o**	**2a**	24	 **3oa**	61
4	**1a**	**2b**	24	**3ab** + **3'ab**	64[e] (92:8)
5	**1a**	**2k**	4	 **3ak**	67 (>99:1)
6	**1a**	**2r**	4	 **3ar**	34 (>99:1)
7	**1a**	**2o**	4	 **3ao**	60 (>99:1),
8	**1a**	**2s**	4	 **3as**	46 (>99:1)
9	**1a**	 ***Si*** = $SiMe_2t$-Bu **2t**	4	 **3at**	72 (>99:1)

[a] All the reaction was carried out using allyl cyanide (1.00 mmol), an alkyne (1.00 mmol), $Ni(cod)_2$ (20 μmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (40 μmol), and $AlMe_2Cl$ (60 μmol) in toluene (2.0 mL) at 50 °C. [b] Isolated yields. [c] Determined by ^1H NMR analysis. [d] $Ni(cod)_2$ (0.20 mmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.40 mmol), and $AlMe_2Cl$ (0.60 mmol) were used. [e] Isolated yield of an inseparable mixture of **3ab** and **3'ab**.

Table 8. Nickel/Lewis acid-catalyzed carbocyanation of alkynes using **1g**.[a]



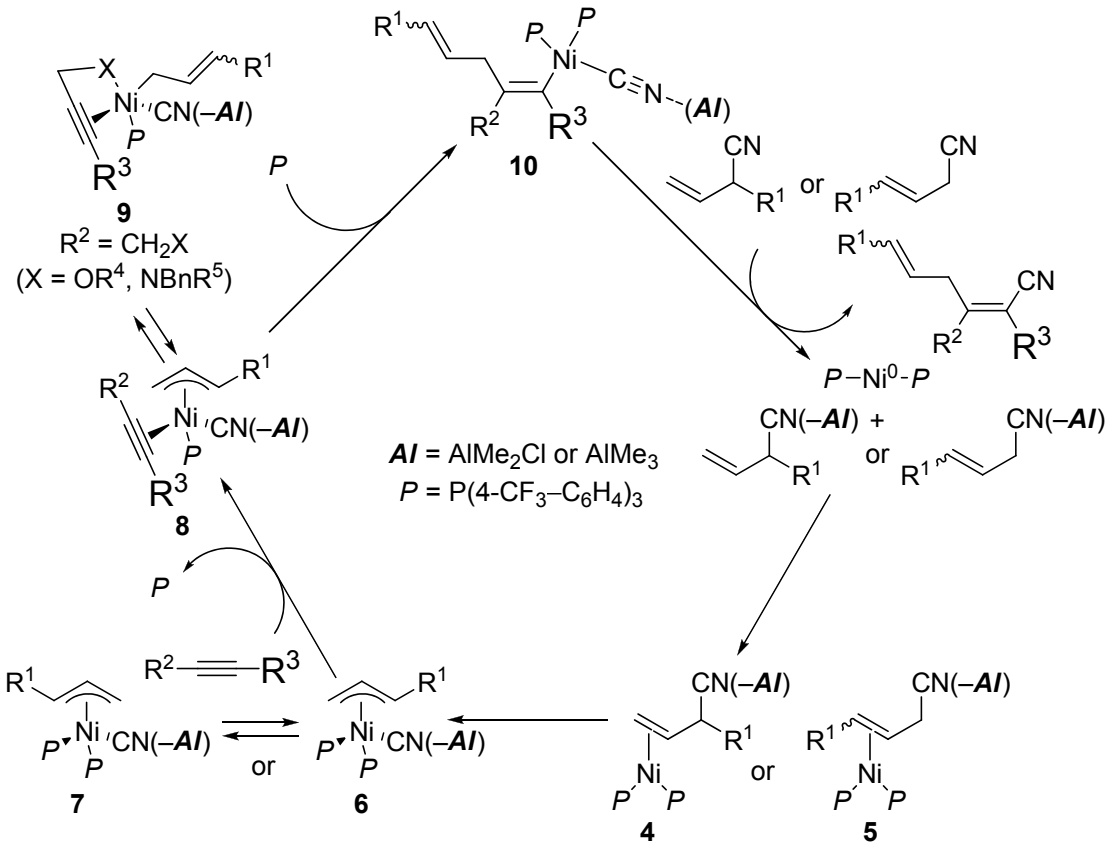
Entry	Alkyne (**2**)	Time (h)	Product(s)	Yield (%)[b] (**3**:**3'**)[c]
1[d]	**2a**	12	**3ga**	80
2	**2k**	2	**3gk** + **3'gk**	62 (98:2)
3[e]	 **2r**	7	 **3gr**	58 (>99:1)
4	**2o**	1	**3go** + **3'go**	60 (98:2)
5	**2p**	2	**3gp** + **3'gp**	59 (97:3)
6	 ***Si*** = $SiMe_2t$-Bu **2u**	1	 **3gu** **3'gu**	36 (99:1)

[a] All the reaction was carried out using **1g** (1.00 mmol), an alkyne (1.00 mmol), $Ni(cod)_2$ (50 μmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (0.100 mmol), and $AlMe_3$ (20 μmol) in toluene (1.5 mL) at 50 °C. [b] Isolated yields of an inseparable mixture of two regioisomers. [c] Determined by ^1H NMR analysis. [d] $Ni(cod)_2$ (20 μmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (40 μmol), and $AlMe_2Cl$ (80 μmol) were used. [e] **2r** (3.0 mmol) was used.

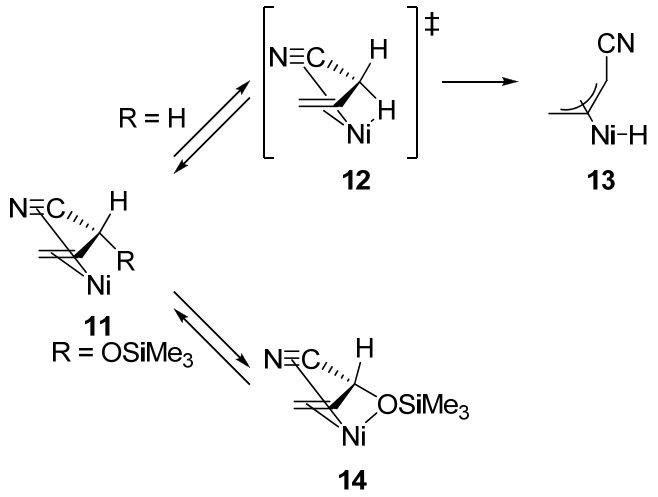
Mechanism of allylcyanation reaction

Catalytic cycle of the present allylcyanation reaction should be initiated by coordination of the double bond of allyl cyanides to nickel(0) to give **4** or **5** followed by oxidative addition of the C–CN bond to nickel(0) to give π-allylnickel intermediate **6** or **7** (Scheme 1). The intermediacy of the π-allylnickel species **6** and **7** is fully supported by literature precedents as well as the experimental results for the reactions of crotyl and

3-buten-2-yl cyanides (entries 1 and 2 of Table 2). With γ-substituted allyl cyanides, the resulting π-allylnickel **7** would be in equilibrium with **6** through isomerization via σ-allyl complex and rotation. One of the phosphine ligands in **6** or **7** may be dissociatively substituted by an alkyne to give **8**. Migratory insertion of alkynes into the allyl–Ni bond in **8** would take place to make bonds at less hindered carbons of the allyl and alkyne both bound to the nickel center, giving **10** with high regioselectivity observed especially with alkynes having sterically biased substituents. High regioselectivity attained with a propargylic heteroatom (entries 6–9 of Table 4) may be ascribed to formation of σ-allylnickel **9** by intramolecular coordination of a heteroatom to the nickel center. Facile isomerization of a η^3-allyl ligand to a η^1-allyl one may direct this particular coordination of the alkynes. An allyl substituent appears to further enhance the directing effect. Reductive elimination of alkenylnickel intermediate **10** gives *cis*-allylcyanation products and regenerates nickel(0). With α-siloxyallyl cyanides, undesired side reactions derived possibly from allylic C–H oxidative addition through transition state **12** (Scheme 2)[7c] are likely suppressed by coordination of the oxygen to nickel in **14**. This additional coordinating site of α-siloxyallyl cyanides may also accelerate and/or strengthen their complexation to nickel(0), preventing alkynes to undergo undesired trimerization and/or oligomerization. Thus, the successful allylcyanation of terminal alkynes with α-siloxyallyl cyanides should be ascribed to the presence of the oxygen functionality. The pronounced effect of phosphine ligands with highly electron-withdrawing aryl groups in the present allylcyanation reaction contrasts sharply to other nickel-catalyzed carbocyanation reactions, wherein phosphine ligands with electron-donating alkyl groups are favored.[6] The oxidative addition of allyl cyanides to nickel(0) is probably very fast compared with other nitriles, and, thus, the turnover limiting step may lie in other elemental steps. Especially, reductive elimination of alkenyl–CN bonds would be facilitated by phosphine ligands with a large π-accepting character. Accordingly, Lewis acid cocatalysts may also accelerate the reductive elimination,[13] ligand substitution, and/or migratory insertion of alkynes as well as oxidative addition of allyl cyanides.[7c]



Scheme 1. Plausible mechanism of allylcyanation of alkynes.



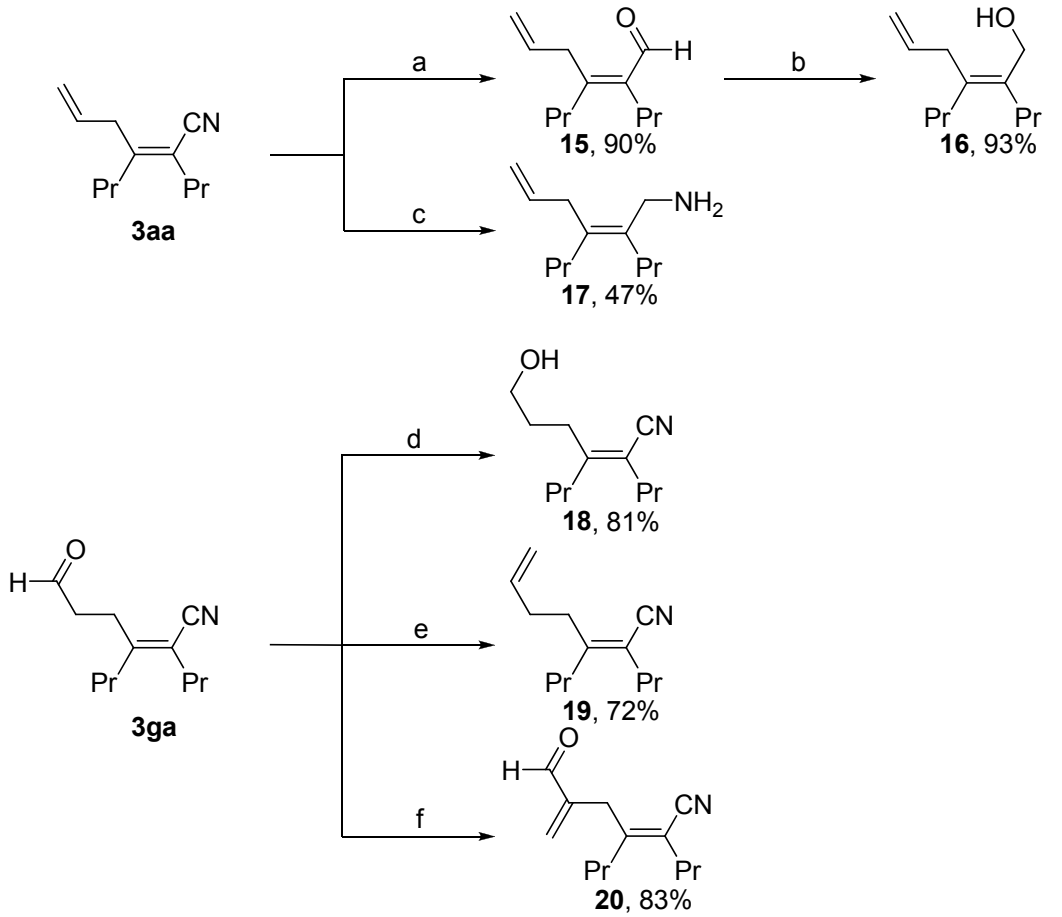
Scheme 2. Oxidative addition of allylic C–H bonds of allyl cyanides to nickel(0).

Transformations of allylcyanation products

Synthetic utility of the allylcyanation products was briefly examined and

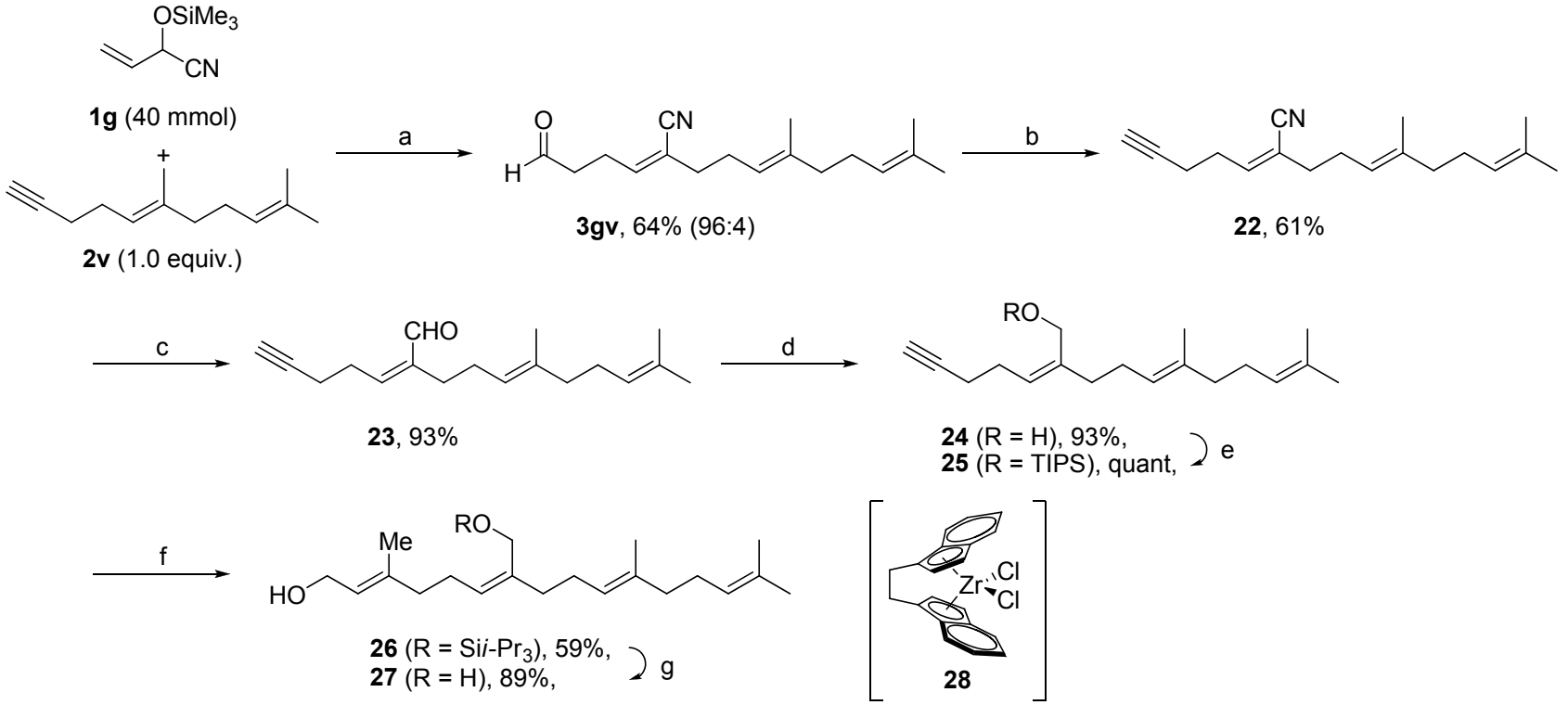
summarized in Scheme 3. The cyano group in **3aa** was reduced to give the corresponding substituted acrolein **15** and then allylic alcohol **16**. Highly substituted allylamine **17** was also available from **3aa**. The formyl group of **3ga** was reduced or methylenated[14] to give alcohol **18** and **19**, the latter serving as a formal homoallycyanation product. α-Methylenation of **3ga** proceeded through aldol-type condensation to give α-substituted acrolein **20** without affecting the configuration of the original C=C bond.[15]

The carbocyanation of terminal alkynes was successfully applied to regio- and stereoselective construction of one of the tri-substituted ethene units in plaunotol (**27**), an antibacterial natural product active against *Helicobacter pylori*.[16,17] Nickel/$AlMe_3$-catalyzed *cis*-carbocyanation of alkyne **2v** with **1g** proceeded with excellent regioselectivity in 64% yield even in gram scale with two internal double bonds intact. The formyl group of aldehydes **3gv** and regioisomer **3'gv** (at most 4%) was transformed to terminal alkyne **22** by the Ohira-Bestmann protocol.[18] The isomer derived from **3'gv** was removed at this stage by silica gel column chromatography. The cyano group was reduced to give substituted allylic alcohol **24** through aldehyde **23** with complete retention of its stereochemistry. The hydroxyl group was silylated with TIPSCl, and the terminal alkyne moiety was subjected to the regio- and stereoselective Negishi methylalumination reaction according to a modified protocol reported by Lipshutz using **28**[19,20] to construct another tri-substituted double bond by treatment of the resulting alkenylaluminum species with paraformaldehyde all in one-pot. Deprotection of the TIPS group gave plaunotol (**27**).



Reagents and conditions: (a) DIBAL-H, toluene, –78 °C, 1.5 h, then SiO_2; (b) $LiAlH_4$, THF, rt, 10 min; (c) DIBAL-H, toluene, –78 °C, 1.5 h, then $NaBH_4$, MeOH, 0 °C, 30 min; (d) $NaBH_4$, MeOH, 0 °C, 1 h; (e) $IZnCH_2ZnI$, THF, rt, 30 min; (f) HCHO aq., pyrrolidine, $EtCO_2H$, *i*-PrOH, 45 °C, 24 h.

Scheme 3. Transformations of allylcyanation products.



Reagents and conditions: (a) $Ni(cod)_2$ (2 mol%), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (4 mol%), $AlMe_3$ (8 mol%), toluene, 35 °C, 8 h, then 1 M HCl aq., THF, 0 °C to rt; (b) $Me(CO)C(N_2)P(O)(OMe)_2$ (**21**), K_2CO_3, MeOH, 0 °C to rt 24 h; (c) DIBAL-H, toluene, –78 °C, 1.5 h, then SiO_2; (d) $LiAlH_4$, THF, 0 °C to rt 20 min; (e) TIPSCl, ImH, DMF, rt, 3 h; (f) $AlMe_3$, **28** (5 mol%), MAO (5 mol%), rt, 48 h, then *n*-BuLi, $(HCHO)_n$, THF, rt, 1.5 h; (g) TBAF, THF, rt, 12 h.

Scheme 4. Synthesis of plaunotol.

Conclusion

In summary, stereo- and regioselective allylcyanation of alkynes has been demonstrated with a $Ni(cod)_2/P(4\text{-}CF_3\text{–}C_6H_4)_3$ catalyst to give highly substituted and functionalized 1,4-dienenitriles. α-Siloxyallyl cyanides are also shown to participate in the transformation, allowing simultaneous introduction of a cyano and 3-oxo-propyl units. Use of Lewis acid cocatalysts is disclosed to significantly improve the reaction efficiency by reducing catalyst loading, achieving stoichiometric reaction, and expanding substrate scope. The resulting adducts have been shown to undergo various transformations based on cyano, allyl, and carbonyl functionalities. Finally, the reaction was applied to synthesis of tri-substituted double bond in plaunotol in a high regio- and stereoselective manner.

Experimental Section

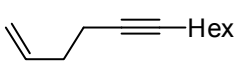
General remarks compatible to all the experimental part in the present Thesis

All manipulations of oxygen- and moisture-sensitive materials were conducted with a standard Schlenk technique or in a dry box under an argon atmosphere. Flash column chromatography was performed using Kanto Chemical silica gel (spherical, 40–50 μm). Analytical thin layer chromatography (TLC) was performed on Merck Kieselgel 60 F_{254} (0.25 mm) plates. Visualization was accomplished with UV light (254 nm) and/or an aqueous alkaline $KMnO_4$ solution followed by heating. Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Varian Mercury 400 (^{1}H NMR, 400 MHz; ^{13}C NMR, 101 MHz), or a Varian Gemini 300 (^{31}P NMR, 121 MHz) spectrometer with solvent resonance as the internal standard (^{1}H NMR, $CHCl_3$ at 7.26 ppm, C_6D_5H at 7.15 ppm, (O)S(CD_3)(CD_2H) at 2.48 pm; ^{13}C NMR, $CDCl_3$ at 77.0 ppm, C_6D_6 at 128.62 ppm, DMSO-d_6 at 40.45 ppm) or (^{31}P NMR, phosphoric acid at 0 ppm) as an external standard. Melting points were determined using a YANAKO MP-500D. Elemental analyses were performed by Elemental Analysis Center of Kyoto University. High-resolution mass spectra were obtained with a JEOL JMS-700 (EI) or JEOL JMS-HX110A (FAB+) spectrometer. Preparative recycling gel permeation chromatography (GPC) and preparative recycling silica gel chromatography were performed with a JAI LC-908 chromatograph equipped with JAIGEL-1H and -2H (chloroform as an eluent) and JAIGEL-SIL or Nacalai tesque 5SL-II (hexane–ethyl acetate as an eluent). GC analysis was performed on a Shimadzu GC 2014 equipped with an ENV-1 column (Kanto Chemical, 30 m x 0.25 mm, pressure = 31.7 kPa, detector = FID, 290 °C) with a helium gas as a carrier. Unless otherwise noted, commercially available reagents were used without purification. Toluene was distilled from sodium/benzophenone ketyl or purchased from Kanto Chemical and degassed by purging vigorously with argon for 20 min and further purified by passing through activated alumina under positive argon pressure as described by Grubbs et al. [21]

Chemicals. Anhydrous CH_3CN was purchased from Nacalai Tesque and bubbled vigorously with an argon gas for 20 min before use. Allyl cyanides, **1d** [from (*E*)-4,4-dimethyl-2-pentenyl methyl carbonate],[22] **1e**,[21] **1g**,[11a] **1h**,[11b] **1i**,[11b] **1j** (from phenyl vinyl ketone at 0 °C),[11b] and **1k**,[11c] **1l**,[11c] **1m**,[11a] **1n**,[11d] and alkyne **2p**[23b] were

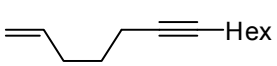
prepared according to the respective literature procedure.

Preparation of dodec-1-en-5-yne (2e).[12] To a solution of 1-octyne (2.2 g, 21 mmol) in THF (50 mL) was added a 1.6 M solution of *n*-BuLi in hexane (13.3 mL, 21 mmol) at –40 °C, and the resulting mixture was stirred at 0 °C before addition of 4-bromo-1-butene (2.7 g, 20 mmol) at –40 °C. Stirring was continued at room temperature for 120 h, and the solution was diluted with diethyl ether, washed with water and brine, and dried over anhydrous $MgSO_4$. After removal of the solvents *in vacuo*, the residue was purified by Kugelrohr distillation (0.1 mmHg, 60 °C) to give **2e**



(0.52 g, 16%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.91–5.83 (m, 1H), 5.09–5.05 (m, 1H), 5.03–5.00 (m, 1H), 2.26–2.23 (m, 4H), 2.17–2.13 (m, 2H), 1.51–1.44 (m, 2H), 1.41–1.24 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.5, 115.5, 81.0, 79.6, 33.6, 31.6, 29.3, 28.8, 22.8, 19.0, 18.9, 14.3.

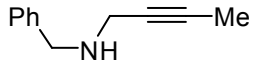
Preparation of tridec-1-en-6-yne (2f).[12] Following the procedure for **2e** and starting from 1-octyne (2.1 g, 20 mmol), a 1.6 M solution of *n*-BuLi in hexane (12.5 mL, 20 mmol), and 5-bromo-1-pentene (2.8 g, 19.0 mmol) in THF (50 mL) at reflux temperature for 48 h, **2f** (1.28 g, 38%) was isolated as a colorless oil by Kugelrohr



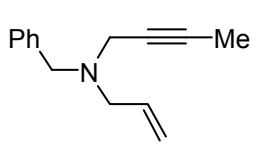
distillation (1 mmHg, 85 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.85–5.76 (m, 1H), 5.06–5.01 (m, 1H), 4.99–4.96 (m, 1H), 2.19–2.12 (m, 6H), 1.58 (quint, *J* = 7.0 Hz, 2H), 1.48 (quint, *J* = 7.0 Hz, 2H), 1.42–1.24 (m, 6H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.4, 115.1, 80.8, 80.0, 33.0, 31.6, 29.3, 28.8, 28.54, 22.8, 19.0, 18.4, 14.3.

Preparation of *N*-benzylbut-2-yn-1-amine.[23b] To a suspension of NaH (0.96 g, 40 mmol) in THF (50 mL) was added benzylamine (8.6 g, 80 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 10 min before addition of 1-bromo-2-butyne (2.7 g, 20 mmol) at 0 °C. Stirring was continued at room temperature for 7 h, and the mixture was quenched with water at 0 °C. The whole was diluted with diethyl ether, washed with a saturated $NaHCO_3$ aqueous solution, water, and then brine,

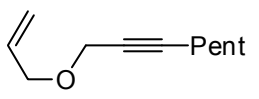
and dried over anhydrous $MgSO_4$. After removal of the solvents *in vacuo*, the residue was purified by flash column chromatography (hexane–EtOAc = 5 : 1) on silica gel to give the title compound (2.2 g, 69%) as a colorless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.30 (m, 5H), 3.83 (s, 2H), 3.35 (q, J = 2.3 Hz, 2H), 1.83 (t, J = 2.3 Hz, 3H), 1.60 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 128.3, 127.0, 79.1, 77.1, 52.5, 37.8, 3.5.



Preparation of *N*-allyl-*N*-benzyl-2-but-2-yn-1-amine (2g). To a suspension of NaH (0.35 g, 15.0 mmol) in THF (50 mL) was added *N*-Benzylbut-2-yn-1-amine (2.2 g, 14.0 mmol) at 0 °C, and the resulting mixture was stirred at room temperature for 1 h before addition of allyl bromide (1.67 g, 14.0 mmol) at 0 °C. Stirring was continued at room temperature for 24 h, and the reaction was quenched with water at 0 °C. The whole solution was diluted with diethyl ether, washed with a saturated $NaHCO_3$ aqueous solution, water, and brine, and then dried over anhydrous $MgSO_4$. After removal of the solvents *in vacuo*, the residue was purified by flash column chromatography (hexane–EtOAc = 5 : 1) on silica gel followed by Kugelrohr distillation (0.1 mmHg, 130 °C) to give **2g** (2.0 g, 73%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.21 (m, 5H), 5.97–5.82 (m, 1H), 5.27 (dq, J = 17.1, 1.7 Hz, 1H), 5.17 (d, J = 10.2 Hz, 1H), 3.63 (s, 2H), 3.26 (q, J = 2.3 Hz, 2H), 3.16 (d, J = 6.4 Hz, 2H), 1.89 (t, J = 2.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.6, 135.7, 129.0, 128.1, 126.9, 117.6, 80.7, 73.8, 57.2, 56.7, 41.9, 3.70; IR (neat) 3065, 2918, 2814, 1643, 1495, 1331, 1254, 1123, 1074, 1028, 922, 741, 698 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{17}N$: M^+, 199.1361. Found: *m*/*z* 199.1351.



Preparation of allyl 2-oct-2-ynyl ether (2i).[23b] Following the procedure for **2g**, the reaction using NaH (1.06 g, 44 mmol), 2-octyn-1-ol (5.0 g, 40 mmol), and allyl bromide (5.8 g, 48 mmol) in THF (30 ml) gave **2i** (5.4 g, 81%) as a colorless oil after Kugelrohr distillation (1.0 mmHg, 90 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.97–5.89 (m, 1H), 5.33–5.29 (m, 1H), 5.23–5.20 (m, 1H), 4.15 (t, J = 2.0 Hz, 2H), 4.07–4.04 (m, 2H), 2.22 (tt, J = 7.0, 2.0 Hz, 2H), 1.56–1.49 (m, 2H), 1.40–1.24 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.4,



117.9, 87.4, 76.0, 70.6, 58.0, 31.3, 28.5, 22.4, 19.0, 14.2.

Nickel-catalyzed allylcyanation of 4-octyne (2a). ***A general procedure.***

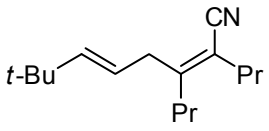
In a dry box, an allyl cyanide (4.0 mmol) and **2a** (110 mg, 1.00 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (92 mg, 0.20 mmol) in CH_3CN (2.0 mL for **1a**–**1c**, **1f**; 1.00 mL for **1d**–**1e**) placed in a vial. The vial was closed and taken outside the dry box and heated at 80 °C for the time specified in Table 2. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding allylcyanation products in yields listed in Table 2.

(*Z*)-2,3-Dipropylhexa-2,5-dienenitrile (3aa). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.73 (ddt, *J* = 16.8, 10.1, 6.8 Hz, 1H), 5.12 (dd, *J* = 16.8, 1.6 Hz, 1H), 5.08 (dd, *J* = 10.1, 1.6 Hz, 1H), 3.12 (d, *J* = 6.8 Hz, 2H), 2.18 (t, *J* = 7.7 Hz, 2H), 2.13 (t, *J* = 8.0 Hz, 2H), 1.57 (sext, *J* = 7.5 Hz, 2H), 1.42 (sext, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.5 Hz, 3H), 0.92 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 133.9, 119.0, 117.4, 111.0, 40.4, 33.2, 31.5, 21.7, 21.1, 14.1, 13.4; IR (neat) 2963, 2934, 2874, 2208, 1638, 1622, 1456, 1437, 1379, 993, 918 cm^{-1}; MS (EI) *m/z* (%) 177 (M^+, 63), 176 (M^+–1, 19), 162 (28), 149 (19), 148 (68), 136 (27), 135 (40), 134 (95), 133 (14), 122 (19), 121 (36), 120 (73), 119 (11), 118 (13), 109 (12), 108 (19), 107 (64), 106 (100), 105 (14), 104 (18), 95 (46), 94 (36), 93 (82), 92 (82), 91 (36), 82 (20), 81 (23), 80 (30), 79 (80), 78 (16), 77 (47), 69 (11), 67 (44), 65 (27), 55 (25), 54 (19), 53 (20), 51 (12). Anal. Calcd for $C_{12}H_{19}N$: C, 81.30; H, 10.80. Found: C, 81.05; H, 10.65.

(2*Z*)-2,3-Dipropylhepta-2,5-dienenitrile (3ba, 5*E*/5*Z* = 85 : 15). A colorless oil, R_f 0.16 (hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.55 (dqt, *J* = 15.1, 6.4, 1.3 Hz, 0.85H), 5.52–5.65 (m, 0.15H), 5.36 (dtq, *J* = 15.1, 6.8, 1.5 Hz, 0.85H), 5.40–5.29 (m, 0.15H), 3.16 (d, *J* = 7.3 Hz, 0.30H), 3.05 (d, *J* = 6.8 Hz, 1.70H), 2.21–2.10 (m, 4H), 1.70 (ddt, *J* = 7.0, 1.9, 0.9 Hz, 0.45H), 1.67 (dq, *J* = 6.4, 1.5 Hz, 2.55H), 1.59 (sext, *J* = 7.5 Hz, 2H), 1.41 (sext,

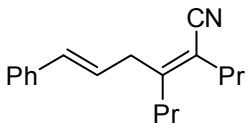
J = 7.6 Hz, 2H), 0.94 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR [for (*2Z,5E*)-**3ba,** 101 MHz, $CDCl_3$] δ 158.0, 128.2, 126.5, 119.2, 110.2, 39.3, 33.2, 31.5, 21.7, 21.2, 17.9, 14.1, 13.5; IR (neat) 2963, 2934, 2874, 2208, 1622, 1456, 1379, 1082, 966 cm^{-1}. Anal. Calcd for $C_{13}H_{21}N$: C, 81.61; H, 11.06. Found: C, 81.81; H, 11.24.

(2*Z*,5*E*)-7,7-Dimethyl-2,3-dipropylocta-2,5-dienenitrile (3da). A colorless oil, R_f 0.33



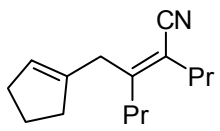
(hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (dt, J = 15.4, 1.3 Hz, 1H), 5.23 (dt, J = 15.6, 7.0 Hz, 1H), 3.06 (d, J = 7.0 Hz, 2H), 2.18 (t, J = 7.6 Hz, 2H), 2.11 (t, J = 8.0 Hz, 2H), 1.58 (sext, J = 7.5 Hz, 2H), 1.41 (sext, J = 7.5 Hz, 2H), 0.99 (s, 9H), 0.94 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 144.8, 120.1, 119.2, 110.1, 39.6, 33.1, 33.0, 31.5, 29.5, 21.7, 21.2, 14.1, 13.4; IR (neat) 2961, 2872, 2208, 1464, 1364, 972, 471 cm^{-1}. Anal. Calcd for $C_{16}H_{27}N$: C, 82.34; H, 11.66. Found: C, 82.55; H, 11.49.

(2*Z*,5*E*)-2,3-Dipropyl-6-phenylhexa-2,5-dienenitrile (3ea). A colorless oil, R_f 0.18



(hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 4H), 7.23 (tt, J = 7.1, 1.5 Hz, 1H), 6.49 (d, J = 15.7 Hz, 1H), 6.12 (dt, J = 15.7, 7.1 Hz, 1H), 3.30 (d, J = 7.1 Hz, 2H), 2.27–2.15 (m, 4H), 1.60 (sext, J = 7.5 Hz, 2H), 1.47 (sext, J = 7.7 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 137.0, 132.6, 128.5, 127.4, 126.2, 125.6, 119.1, 111.0, 39.6, 33.3, 31.6, 21.7, 21.2, 14.1, 13.5; IR (neat) 3026, 2963, 2932, 2872, 2206, 1622, 1497, 1448, 1381, 1113, 966, 912, 735, 694 cm^{-1}. Anal. Calcd for $C_{18}H_{23}N$: C, 85.32; H, 9.15. Found: C, 85.58; H, 9.44.

(*Z*)-3-(Cyanopent-1-enyl)methyl-2-propylhex-2-enenitrile (3fa). A colorless oil, R_f



0.21 (hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ; 5.40 (t, J = 2.0 Hz, 1H), 3.17 (s, 2H), 2.35–2.28 (m, 2H), 2.27–2.18 (m, 4H), 2.11 (t, J = 7.9 Hz, 2H), 1.87 (quint, J = 7.5 Hz, 2H), 1.60 (sext, J = 7.4 Hz, 2H), 1.41 (sext, J = 7.6 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 140.3, 126.5, 119.2, 110.9, 38.2,

34.9, 33.4, 32.5, 31.7, 23.5, 21.9, 21.5, 14.3, 13.6; IR (neat) 2961, 2932, 2872, 2847, 2208, 1624, 1466, 1379, 1340, 1296, 1084, 1040, 916, 735 cm^{-1}. Anal. $C_{15}H_{23}N$: C, 82.89; H, 10.67. Found: C, 82.73; H, 10.62.

(*Z*)-3-Methyl-2-phenylhexa-2,5-dienenitrile (3ab). A colorless oil, R_f 0.18 (hexane–ethyl acetate = 50 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.43–7.29 (m, 5H), 5.93–5.81 (m, 1H), 5.29–5.17 (m, 2H), 3.33 (dt**,** *J* = 6.8, 1.4 Hz, 2H), 1.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.7, 133.8, 133.0, 129.0, 128.5, 128.2, 118.4, 118.1, 111.5, 42.9, 19.6; IR (neat) 3061, 2924, 2212, 1618, 1493, 1443, 1377, 991, 920, 766, 725, 700 cm^{-1}. Anal. $C_{13}H_{13}N$: C, 85.21; H, 7.15. Found (as a mixture with **3'ab**): C, 85.47; H, 7.26.

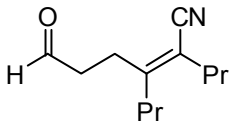
(*E*)-2-Methyl-3-phenylhexa-2,5-dienenitrile (3'ab). A colorless oil, R_f 0.18 (hexane–ethyl acetate = 50 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.46–7.29 (m, 3H), 7.12 (dt, *J* = 6.6, 1.7 Hz, 2H), 5.73–5.61 (m, 1H), 5.13–5.00 (m, 2H), 3.48 (dd, *J* = 6.8, 0.9 Hz, 2H), 1.85 (t, *J* = 0.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 137.7, 132.9, 128.3, 128.2, 127.5, 119.4, 117.6, 106.5, 42.7, 17.9; IR (neat) 2964, 2355, 2332, 2216, 1558, 1258, 1096, 1015, 920, 797, 696 cm^{-1}.

Carbocyanation of alkynes with α-siloxyallyl cyanides. ***A general procedure.***

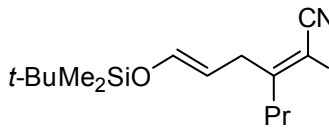
In a dry box, an α-siloxyallyl cyanides (1.50 mmol for the reaction with internal alkynes; 1.00 mmol for the reaction with terminal alkynes) and an alkyne (1.00 mmol of internal alkynes or 2.0 mmol of terminal alkynes) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (92 mg, 0.20 mmol) in CH_3CN (1.00 mL) in a vial. The vial was closed, taken outside the dry box, and heated at 80 °C for the time specified in Tables 3–5. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was dissolved in THF (10 mL) and treated with a 1 M HCl aqueous solution (5.0 mL) at 0 °C. The mixture was stirred at room temperature overnight and extracted with Et_2O for three times. Combined organic layers were

washed with water and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography (**3gc** was purified by Kugelrohr distillation) to give the corresponding allylcyanation products in yields listed in Tables 3–5. In some cases, regioisomers were further separated by preparative recycling silica gel chromatography.

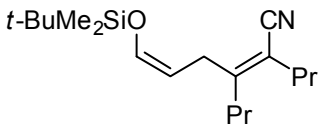
(*Z*)-6-Oxo-2,3-dipropylhex-2-enenitrile (3ga). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 2.74–2.58 (m, 4H), 2.17 (t, *J* = 7.7 Hz, 2H), 2.13 (t, *J* = 7.9 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.5 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 157.5, 118.7, 111.5, 42.2, 33.4, 31.4, 28.2, 21.6, 21.3, 14.0, 13.4; IR (neat) 2963, 2934, 2874, 2206, 1726, 1624, 1456, 1381, 1123, 1088, 1049 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91. Found: C, 74.64; H, 9.85.



(2*Z*,5*E*)-6-*tert*-Butyldimethylsiloxy-2,3-dipropylhexa-2,5-dienenitrile [(*E*)-3ha]. A colorless oil, R_f 0.31 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (dt, *J* = 11.7, 1.2 Hz, 1H), 4.93 (dt, *J* = 11.7, 7.6 Hz, 1H), 2.94 (d, *J* = 7.5 Hz, 2H), 2.17 (t, *J* = 7.6 Hz, 2H), 2.13 (t, *J* = 7.9 Hz, 2H), 1.62–1.50 (m, 2H), 1.41 (sext, *J* = 7.5 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 142.7, 119.1, 109.9, 107.0, 34.1, 32.9, 31.5, 25.6, 21.7, 21.1, 18.3, 14.1, 13.5, –5.3; IR (neat) 2961, 2932, 2858, 2206, 1661, 1464, 1256, 1196, 1169, 928, 839, 783 cm^{-1}. Anal. Calcd for $C_{18}H_{33}NOSi$: C, 70.30; H, 10.82. Found [as a mixture with (*Z*)-**3ha**]: C, 70.56; H, 11.02.

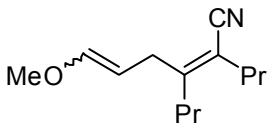


(2*Z*,5*Z*)-6-*tert*-Butyldimethylsiloxy-2,3-dipropylhexa-2,5-dienenitrile [(*E*)-3ha]. A colorless oil, R_f 0.31 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (dt, *J* = 5.7, 1.4 Hz, 1H), 4.39 (td, *J* = 7.4, 5.7 Hz, 1H), 3.20 (d, *J* = 7.5 Hz, 2H), 2.17 (t, *J* = 7.3 Hz, 2H), 2.13 (t, *J* = 7.9 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.44 (sext, *J* =

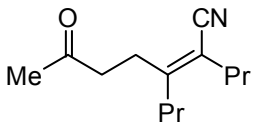


7.5 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.93 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 140.5, 119.4, 109.5, 105.5, 33.0, 31.5, 30.6, 25.6, 21.7, 21.3, 18.2, 14.1, 13.5, –5.4; IR (neat) 2961, 2932, 2860, 2206, 1651, 1258, 1103, 837, 781 cm^{-1}.

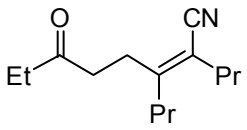
(2*Z*)-6-Methoxy-2,3-dipropylhexa-2,5-dienenitrile (3ia, 5*E*/5*Z* = 22 : 78). A colorless oil, R_f 0.24 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (d, *J* = 12.6 Hz, 0.78H), 5.99 (dt, *J* = 6.4, 1.6 Hz, 0.22H), 4.66 (dt, *J* = 12.6, 7.5 Hz, 0.78H), 4.30 (td, *J* = 8.8, 4.8 Hz, 0.22H), 3.61 (s, 0.66H), 3.52 (s, 2.34H), 3.16 (d, *J* = 7.2 Hz, 0.44H), 2.98 (d, *J* = 7.5 Hz, 1.56H), 2.20–2.11 (m, 4H), 1.60–1.54 (m, 2H), 1.46–1.39 (m, 2H), 0.97–0.91 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 158.4, 149.0, 147.8, 119.0, 118.8, 109.7, 109.4, 101.8, 98.3, 59.3, 55.7, 34.2, 32.8, 32.6, 31.3, 30.6, 21.5, 21.0, 20.9, 13.91, 13.87, 13.2, 13.1; IR (neat) 2934, 2874, 2833, 2206, 1651, 1624, 1464, 1381, 1213, 1157, 1134, 1109, 937, 797, 741 cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21. Found: C, 75.30; H, 9.96.



(*Z*)-6-Oxo-2,3-dipropylhept-2-enenitrile (3ja). A colorless oil, R_f 0.17 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66–2.57 (m, 4H), 2.18 (s, 3H), 2.17 (t, *J* = 7.6 Hz, 2H), 2.12 (t, *J* = 7.9 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.7 Hz, 2H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.8, 158.2, 118.8, 110.9, 41.8, 33.4, 31.3, 29.7, 29.6, 21.6, 21.2, 14.0, 13.3; IR (neat) 2934, 2874, 2206, 1715, 1624, 1456, 1362, 1163 cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO$: C, 75.32; H, 10.21. Found: C, 75.30; H, 9.96.



(*Z*)-6-Oxo-2,3-dipropyloct-2-enenitrile (3ka). A colorless oil, R_f 0.37 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67–2.53 (m, 4H), 2.47 (q, *J* = 7.3 Hz, 2H), 2.17 (t, *J* = 7.6 Hz, 2H), 2.12 (t, *J* = 7.9 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.6 Hz, 2H), 1.07 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR



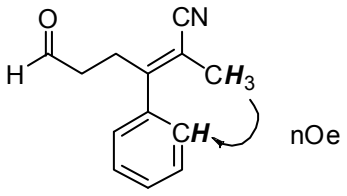
(101 MHz, $CDCl_3$) δ 209.5, 158.4, 118.8, 110.8, 40.5, 35.6, 33.4, 31.3, 29.8, 21.5, 21.2, 13.9, 13.3, 7.6; IR (neat) 2964, 2936, 2874, 2206, 1717, 1458, 1111, 735 cm^{-1}. Anal. Calcd for $C_{14}H_{23}NO$: C, 75.97; H, 10.47. Found: C, 75.80; H, 10.24.

(*Z*)-6-Oxo-6-phenyl-2,3-dipropylhex-2-enenitrile (3la). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.1 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 3.15 (t, *J* = 7.9 Hz, 2H), 2.81 (t, *J* = 7.9 Hz, 2H), 2.25–2.14 (m, 4H), 1.58 (sext, *J* = 7.5 Hz, 2H), 1.47 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.4, 158.6, 136.4, 133.2, 128.6, 128.0, 118.9, 111.1, 37.2, 33.7, 31.5, 30.3, 21.7, 21.3, 14.1, 13.4; IR (neat) 2963, 2874, 2208, 1686, 1597, 1448, 1205, 735, 691 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NO$: C, 80.26; H, 8.61. Found: C, 80.53; H, 8.55.

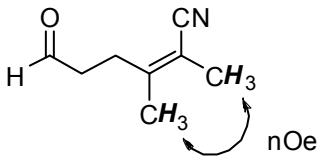
(*Z*)-5-Methyl-6-oxo-2,3-dipropylhex-2-enenitrile (3ma). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.66 (s, 1H), 2.78 (dd, *J* = 13.2, 5.7 Hz, 1H), 2.62–2.52 (m, 1H), 2.49 (dd, *J* = 13.2, 8.4 Hz, 1H), 2.27–2.03 (m, 4H), 1.58 (sext, *J* = 7.5 Hz, 2H), 1.52–1.36 (m, 2H), 1.17 (d, *J* = 7.0 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.1, 156.0, 118.9, 112.7, 45.2. 36.2, 33.2, 31.5, 21.6, 21.3, 14.0, 13.3, 13.2; IR (neat) 2963, 2934, 2874, 2208, 1697, 1634, 1558, 1456, 1379 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{21}NO$: M^+, 207.1623. Found: *m*/*z* 207.1624.

(*Z*)-3-Methyl-6-oxo-2-phenylhex-2-enenitrile (3gb). A pale yellow oil, R_f 0.26 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 7.44–7.25 (m, 5H), 2.91 (t, *J* = 7.4 Hz, 2H), 2.78 (t, *J* = 7.4 Hz, 2H), 1.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 156.1, 133.5, 128.9, 128.5, 128.4, 118.1, 112.0, 41.5, 30.6, 19.5; IR (neat) 3447, 2940, 2210, 1722, 1616, 1493, 1447, 1377, 1136, 766, 700 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{13}NO$: M^+, 199.0997. Found: *m*/*z* 199.0991.

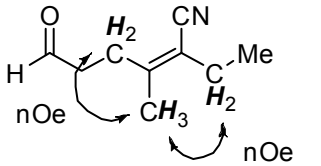
(*E*)-2-Methyl-6-oxo-3-phenylhex-2-enenitrile (3'gb). A pale yellow oil, R_f 0.29 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (t, *J* = 1.1 Hz, 1H), 7.44–7.33 (m, 3H), 7.12–7.06 (m, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 2.47 (td, *J* = 7.6, 1.1 Hz, 2H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0, 156.4, 136.9, 128.8, 128.7, 127.5, 119.1, 107.1, 41.5, 30.7, 17.7; IR (neat) 2961, 2924, 2856, 2212, 1722, 1493, 1441, 702 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{13}NO$: M^+, 199.0997. Found: *m*/*z* 199.0997.



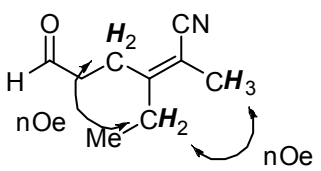
(*Z*)-2,3-Dimethyl-6-oxohex-2-enenitrile (3gc). A colorless oil, bp 100 °C (1.0 mmHg), R_f 0.14 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 3.81 (t, *J* = 7.2 Hz, 2H), 2.67–2.60 (m, 2H), 1.88 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 153.7, 119.2, 105.1, 41.6, 30.4, 18.1, 16.2; IR (neat) 3420, 2932, 2210, 1722, 1636, 1447, 1387, 1138, 733 cm^{-1}. Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08. Found: C, 69.77; H, 7.82.



(*Z*)-2-Ethyl-3-methyl-6-oxohex-2-enenitrile (3gd). A colorless oil, R_f 0.38 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (t, *J* = 1.4 Hz, 1H), 2.76–2.68 (m, 2H), 2.67–2.60 (m, 2H), 2.22 (q, *J* = 7.6 Hz, 2H), 1.83 (s, 3H), 1.12 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 152.6, 118.5, 112.6, 41.8, 30.6, 23.3, 17.9, 12.6; IR (neat) 2974, 2936, 2876, 2829, 2729, 2208, 1724, 1630, 1452, 1410, 1387, 1067, 733 cm^{-1}. Anal. Calcd for $C_9H_{13}NO$: C, 71.49 H, 8.67. Found (as a mixture with **3'gd**): C, 71.55; H, 8.75.

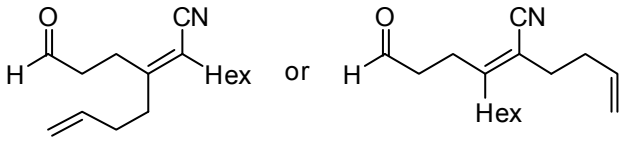


(*Z*)-3-Ethyl-2-methyl-6-oxohex-2-enenitrile (3'gd). A colorless oil, R_f 0.33 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (t, *J* = 1.3 Hz, 1H), 2.75–2.68 (m, 2H), 2.66–2.59 (m, 2H), 2.18 (q, *J* = 7.6 Hz, 2H), 1.89 (s, 3H), 1.03 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.3, 159.2, 119.4,



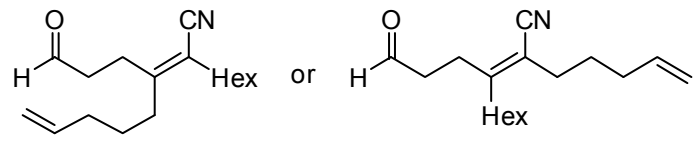
105.1, 42.0, 27.8, 24.7, 15.8, 11.8; IR (neat) 2974, 2937, 2878, 2829, 2729, 2210, 1724, 1632, 1450, 1410, 1389, 733 cm^{-1}.

(*Z*)-7(8)-Cyano-8(7)-(3-oxoprop-1-yl)-dodeca-7,11-diene (3ge or 3'ge). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 5.82–5.66 (m, 1H), 5.12–4.96 (m, 2H), 2.73–2.57 (m, 4H), 2.33–2.22 (m, 4H), 2.13 (t, *J* = 7.7 Hz, 2H), 1.43–1.18 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 158.1, 136.1, 118.4, 116.1, 110.5, 42.3, 32.5, 31.7, 31.6, 29.4, 29.1, 28.3, 28.0, 22.6, 14.1; IR (neat) 3078, 2930, 2858, 2723, 2251, 2208, 1726, 1641, 1624, 1452, 1410, 1387, 1117, 995, 916, 735, 648 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{25}NO$: M^+, 247.1936. Found: *m*/*z* 247.1927.



A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 5.82–5.68 (m, 1H), 5.11–4.97 (m, 2H), 2.74–2.57 (m, 4H), 2.32–2.07 (m, 6H), 1.60–1.43 (m, 2H), 1.43–1.16 (m, 6H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 156.2, 136.3, 118.5, 116.0, 112.2, 42.3, 32.0, 31.6, 31.0, 29.8, 28.8, 28.5, 28.3, 22.6, 14.2; IR (neat) 3078, 2957, 2930, 2858, 2723, 2208, 1726, 1641, 1624, 1454, 1410, 1387, 995, 916, 731 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{25}NO$: M^+, 247.1936. Found: *m*/*z* 247.1945.

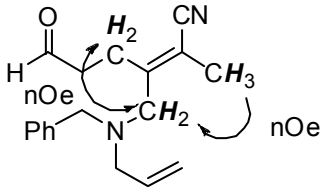
(*Z*)-7(8)-Cyano-8(7)-(3-oxoprop-1-yl)-trideca-7,12-diene (3gf or 3'gf). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 5.85–5.73 (m, 1H), 5.08–4.96 (m, 2H), 2.74–2.59 (m, 4H), 2.21 (t, *J* = 7.7 Hz, 2H), 2.18–2.04 (m, 4H), 1.65 (quint, *J* = 7.6 Hz, 2H), 1.43–1.19 (m, 8H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.0, 157.7, 137.5, 118.6, 115.3, 111.1, 42.3, 33.0, 31.7, 31.6, 29.4, 29.0, 28.4, 28.1, 27.6, 22.6, 14.2; IR (neat) 2930, 2858, 2361, 2343, 2208, 1726, 1624, 1456, 993, 912 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{27}NO$: M^+, 261.2093.



Found: *m*/*z* 261.2099.

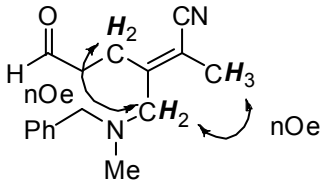
A colorless oil, R_f 0.15 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 5.82–5.71 (m, 1H), 5.07–4.98 (m, 2H), 2.74–2.60 (m, 4H), 2.26–2.12 (m, 4H), 2.08 (q, *J* = 7.1 Hz, 2H), 1.58–1.44 (m, 4H), 1.30 (bs, 6H), 0.89 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 156.9, 137.2, 118.6, 115.6, 111.8, 42.3, 33.6, 31.6, 31.0, 29.7, 28.7, 28.5, 28.3, 27.2, 22.6, 14.1; IR (neat) 2930, 2858, 2723, 2208, 1726, 1641, 1624, 1458, 1410, 1387, 914, 735 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{27}NO$: M^+, 261.2093. Found: *m*/*z* 261.2105.

(*E*)-3-[(*N*-Allyl-*N*-benzylamino)methyl]-2-methyl-6-oxohex-2-enenitrile (3gg). A



colorless oil, R_f 0.18 (hexane–ethyl acetate = 4 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.36–7.22 (m, 5H), 5.92–5.79 (m, 1H), 5.25–5.17 (m, 2H), 3.49 (s, 2H), 3.05 (s, 2H), 2.98 (d, *J* = 7.8 Hz, 2H), 2.80 (t, *J* = 7.8 Hz, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 155.6, 138.5, 134.8, 129.0, 128.4, 127.4, 118.9, 118.5, 107.8, 58.5, 57.1, 52.0, 41.8, 26.8, 16.1; IR (neat) 2928, 2804, 2210, 1724, 1495, 1452, 1369, 1254, 1124, 1072, 1028, 974, 924, 745, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85. Found: C, 76.30; H, 7.64.

(*E*)-3-[(*N*-Benzyl-*N*-methylamino)methyl]-2-methyl-6-oxohex-2-enenitrile (3gh). A



colorless oil, R_f 0.16 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1H), 7.37–7.22 (m, 5H), 3.46 (s, 2H), 2.99 (s, 2H), 2.82 (t, *J* = 7.7 Hz, 2H), 2.51 (td, *J* = 7.8, 1.4 Hz, 2H), 2.13 (s, 3H), 1.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.2, 155.2, 138.2, 129.0, 128.4, 127.4, 119.0, 107.9, 62.5, 55.6, 42.4, 41.9, 27.2, 16.1; IR (neat) 2791, 2359, 2343, 2212, 1722, 1495, 1456, 1020, 743, 700, 669 cm^{-1}; HRMS (FAB) Calcd for $C_{16}H_{21}N_2O$: $[M+H]^+$, 257.1654. Found: *m*/*z* 257.1661.

(*E*)-3-(Allyloxymethyl)-2-methyl-6-oxohex-2-enenitrile (3gi). A colorless oil, R_f 0.04 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 5.93–5.82 (m, 1H), 5.28 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.23 (d, *J* = 10.4 Hz, 1H), 4.06 (s, 2H), 3.95 (d, *J* = 5.5 Hz, 2H), 2.81 (t, *J* = 7.5 Hz, 2H), 2.68 (t, *J* = 8.0 Hz, 2H), 2.21 (t, *J* = 7.7 Hz, 2H), 1.53 (quint, *J* = 7.5 Hz, 2H), 1.38–1.22 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.4, 152.9, 133.7, 118.0, 117.8, 114.1, 71.8, 66.9, 42.1, 30.9, 29.5, 28.0, 26.9, 22.2, 13.8; IR (neat) 2959, 2930, 2860, 2725, 2343, 2212, 1726, 1456, 1410, 1387, 1354, 1084, 991, 930, 733 cm^{-1}; HRMS (FAB+) Calcd for $C_{15}H_{24}NO_2$: $[M+H]^+$, 250.1807. Found: *m*/*z* 250.1814.

(*E*)-3-Methoxymethyl-6-oxo-2-propylhex-2-enenitrile (3gj). A colorless oil, R_f 0.22 (hexane–ethyl acetate = 4 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, *J* = 1.42 Hz, 1H), 4.01 (s, 2H), 3.32 (s, 3H), 2.80 (t, *J* = 7.4 Hz, 2H), 2.67 (t, *J* = 7.3 Hz, 2H), 2.21 (t, *J* = 7.5 Hz, 2H), 1.57 (sext, *J* = 7.4 Hz, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 153.1, 118.0, 113.8, 69.6, 58.7, 42.1, 31.4, 26.7, 21.5, 13.2; IR (neat) 2964, 2934, 2874, 2727, 2212, 1724, 1454, 1383, 1194, 1099, 1061, 912 cm^{-1}. Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78. Found: C, 67.78; H, 8.72.

(*E*)-2-(Methoxymethyl)-6-oxo-3-propylhex-2-enenitrile (3'gj). A colorless oil, R_f 0.09 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 4.04 (s, 2H), 3.39 (s, 3H), 2.78–2.65 (m, 4H), 2.23 (t, *J* = 7.8 Hz, 2H), 1.48 (sext, *J* = 7.7 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 163.0, 118.1, 109.5, 68.5, 58.8, 42.4, 34.6, 28.6, 22.0, 14.5; IR (neat) 2972, 2934, 2370, 2324, 2216, 1724, 1462, 1192, 1096 cm^{-1}; HRMS (EI) Calcd for $C_{11}H_{17}NO_2$: M^+, 195.1259. Found: *m*/*z* 195.1256.

(*Z*)-2-(4-Oxobutylidene)octanenitrile (3gk). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 6.15 (t, *J* = 7.4 Hz, 1H), 2.72–2.59 (m, 4H), 2.18 (t, *J* = 7.6 Hz, 2H), 1.56–1.22 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.5, 145.0, 117.5, 116.6, 42.7, 34.4, 31.6, 28.5, 28.1, 24.2, 22.7, 14.2; IR (neat) 3420, 2930, 2858, 2216, 1717, 1456 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91. Found (as a mixture with **3'gk**): C, 74.31; H, 9.73.

(*Z*)-3-(3-Oxopropyl)non-2-enenitrile (3'gk). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 5.16 (t, *J* = 1.4 Hz, 1H), 2.75–2.63 (m, 4H), 2.17 (td, *J* = 7.6, 1.4 Hz, 2H), 1.49–1.20 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 167.4, 116.7, 96.0, 41.7, 36.3, 31.5, 28.7, 27.03, 27.02, 22.5, 14.0; IR (neat) 2930, 2858, 2216, 1726, 1626, 1454 cm^{-1}.

(*Z*)-2-Isopropyl-6-oxohex-2-enenitrile (3gl, containing 5% of 3'gl). A colorless oil, R_f 0.22 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 0.05H), 9.79 (s, 0.95H), 6.16 (td, *J* = 7.5, 1.1 Hz, 0.95H), 5.19 (d, *J* = 1.2 Hz, 0.05H), 2.69–2.60 (m, 4H), 2.47 (sept, *J* = 6.6 Hz, 1H), 1.13 (d, *J* = 6.7 Hz, 5.7H), 1.09 (d, *J* = 6.8 Hz, 0.3H); ^{13}C NMR (for **3gl**, 101 MHz, $CDCl_3$) δ 200.2, 142.2, 123.0, 116.4, 42.4, 33.1, 23.7, 21.2; IR (neat) 3445, 2966, 2874, 2214, 1726, 1634, 1466, 1389, 1367, 1138, 1036, 656 cm^{-1}; Anal. Calcd for $C_9H_{13}NO$: HRMS (EI) Calcd for $C_9H_{13}NO$: M^+, 151.0997. Found: *m*/*z* 151.1003.

(*Z*)-2-*tert*-Butyl-6-oxohex-2-enenitrile (3gm). A colorless oil, R_f 0.22 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 6.16 (t, *J* = 7.2 Hz, 1H), 2.72–2.60 (m, 4H), 1.16 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.2, 140.4, 127.0, 116.6, 42.5, 34.8, 28.7, 24.0; IR (neat) 2966, 2872, 2214, 1726, 1369, 1140, 1042, 662 cm^{-1}; HRMS (EI) Calcd for $C_{10}H_{15}NO$: M^+, 165.1154. Found: *m*/*z* 165.1161.

(*E*)-6-Oxo-2-trimethylsilylhex-2-enenitrile (3gn). A yellow oil, R_f 0.18 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 6.57 (t, *J* = 7.0 Hz, 1H), 2.79 (q, *J* = 7.0 Hz, 2H), 2.67 (t, *J* = 7.0 Hz, 2H), 0.22 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 159.0, 117.8, 117.2, 42.0, 26.6, –2.2; IR (neat) 2959, 2899, 2827, 2727, 2199, 1726, 1595, 1254, 847, 760 cm^{-1}; HRMS (EI) Calcd for $C_9H_{15}NOSi$: M^+, 181.0923. Found: *m*/*z* 181.0915.

(*Z*)-2-(3-Chloromethyl)-6-oxohex-2-enenitrile (3go). A yellow oil, R_f 0.17 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 6.26 (tt, *J* = 1.3, 7.5 Hz, 1H), 3.55 (t, *J* = 6.2 Hz, 2H), 2.70–2.62 (m, 4H), 2.41 (t, *J* = 7.3 Hz, 2H), 2.07–1.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.9, 146.5, 116.8, 114.3, 43.2, 42.2, 31.1, 30.2, 24.0; IR (neat) 2959, 2845, 2216, 1724, 1445, 914, 733, 650 cm^{-1}. Anal. Calcd for $C_9H_{12}ClNO$: C, 58.23; H, 6.52. Found: C, 57.97; H, 6.50.

Methyl (*Z*)-5-cyano-9-oxonon-5-enoate (3gp, containing 5% of 3'gp). A yellow oil, R_f 0.19 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 0.05H), 9.79 (s, 0.95H), 6.20 (t, *J* = 7.5 Hz, 0.95H), 5.19 (s, 0.05H), 3.68 (s, 3H), 2.73–2.60 (m, 4H), 2.33 (t, *J* = 7.2 Hz, 2H), 2.26 (t, *J* = 7.6 Hz, 2H), 1.87 (quint, *J* = 7.5, Hz, 2H); ^{13}C NMR (for **3gp**, 101 MHz, $CDCl_3$) δ 199.9, 173.1, 145.8, 116.8, 115.1, 51.6, 42.2, 33.2, 32.5, 23.9, 23.0; IR (neat) 2953, 2216, 1732, 1437, 1254, 1200, 1167 cm^{-1}; Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23. Found: C, 63.06; H, 7.28.

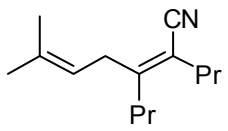
(*Z*)-6-Oxo-2-(4-phthalimidoylbutyl)hex-2-enenitrile (3gq, containing 10% of 3'gq). A yellow oil, R_f 0.19 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 0.10H), 9.78 (s, 0.90H), 7.87–7.79 (m, 2H), 7.75–7.66 (m, 2H), 6.20 (t, *J* = 7.5 Hz, 0.90H), 5.17 (s, 0.10H), 3.68 (t, *J* = 7.0 Hz, 2H), 2.70–2.60 (m, 4H), 2.26 (t, *J* = 7.3 Hz, 2H), 1.86–1.39 (m, 4H); ^{13}C NMR (for **3gq**, 101 MHz, $CDCl_3$)

δ 200.1, 168.3, 145.5, 134.0, 132.0, 123.2, 117.0, 115.5, 42.4, 37.2, 33.5, 27.3, 25.0, 24.0; IR (neat) 2941, 2216, 1771, 1713, 1437, 1396, 1371, 1038, 916, 721, 530 cm^{-1}. Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85. Found: C, 69.86; H, 6.02.

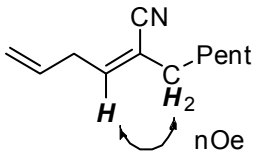
Nickel/$AlMe_2Cl$-catalyzed allylcyanation of alkynes. ***A general procedure.***

In a dry box, an allyl cyanide (1.00 mmol), an alkyne (1.00 mmol), and tetradecane (internal standard, 26 μL, 0.10 mmol) were added sequentially to a solution of $Ni(cod)_2$ (5.6 mg, 20 μmol), $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (18.7 mg, 40 μmol), and a 1.03 M solution of $AlMe_2Cl$ in hexane (58 μL, 60 μmol) in toluene (1.00 mL) placed in a vial. The vial was closed, taken outside the dry box, and heated at 50 °C for the time specified in Table 7. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding carbocyanation products in yields listed in Table 7.

(*Z*)-6-Methyl-2,3-dipropylhepta-2,5-dienenitrile (3oa). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 50 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.06 (tquint, J = 7.3, 1.4 Hz, 1H), 3.10 (d, J = 7.1 Hz, 2H), 2.18 (t, J = 7.6 Hz, 2H), 2.11 (t, J = 7.9 Hz, 2H), 1.73 (d, J = 1.1 Hz, 3H), 1.70 (s, 3H), 1.64–1.52 (m, 2H), 1.43 (sext, J = 7.6 Hz, 2H), 0.94 (q, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 134.3, 119.8, 119.3, 109.6, 35.2, 33.2, 31.6, 25.9, 21.9, 21.4, 18.1, 14.4, 13.6; IR (neat) 2963, 2932, 2874, 2206, 1624, 1456, 1377, 1086, 916, 833, 735 cm^{-1}. Anal. $C_{14}H_{23}N$: C, 81.89; H, 11.29. Found: C, 81.66; H, 11.12.



(*Z*)-2-(But-3-enylidene)octanenitrile (3ak). A colorless oil, R_f 0.24 (hexane–ethyl acetate = 50 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.13 (tt, J = 7.6, 1.3 Hz, 1H), 5.84–5.73 (m, 1H), 5.14–5.06 (m, 2H), 3.10 (t, J = 7.0 Hz, 2H), 2.22 (td, J = 7.6, 1.0 Hz, 2H), 1.62–1.48 (m, 2H), 1.39–1.20 (m, 6H), 0.90 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 133.6, 117.3, 116.7, 115.7, 35.5, 34.3, 31.5, 28.4, 28.0, 22.6, 14.1; IR (neat) 3084, 2930, 2858, 2216, 1639, 1458, 1435, 1379, 1109, 991, 918, 725 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{19}N$: M^+, 177.1517. Found: *m*/*z* 177.1510.



(*Z*)-2-[(Trimethylsilyl)methyl]hexa-2,5-dienenitrile (3ar). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (tt, *J* = 7.7, 1.2 Hz, 1H), 5.83–5.72 (m, 1H), 5.13–5.03 (m, 2H), 3.09 (t, *J* = 7.0 Hz, 2H), 1.69 (d, *J* = 0.9 Hz, 2H), 0.11 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.6, 134.1, 118.3, 116.4, 112.4, 35.7, 24.8, –1.7; IR (neat) 2957, 2899, 2214, 1641, 1418, 1252, 1169, 1101, 991, 914, 854, 735, 700 cm^{-1}; Anal. HRMS (EI) Calcd for $C_{10}H_{17}NSi$: M^+, 179.1130. Found: *m*/*z* 179.1133.

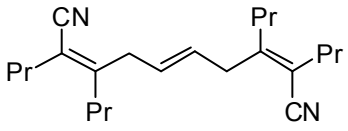
(*Z*)-2-(3-Chloropropyl)hexa-2,5-dienenitrile (3ao). A colorless oil, R_f 0.09 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (t, *J* = 7.6 Hz, 1H), 5.84–5.72 (m, 1H), 5.15–5.07 (m, 2H), 3.56 (t, *J* = 6.2 Hz, 2H), 3.12 (t, *J* = 7.0 Hz, 2H), 2.44 (t, *J* = 7.3 Hz, 2H), 2.02 (quint, *J* = 6.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 133.2, 117.0, 116.9, 113.6, 43.3, 35.6, 31.3, 30.3; IR (neat) 2961, 2216, 1638, 1435, 1292, 993, 920, 652 cm^{-1}; HRMS (EI) Calcd for $C_9H_{12}NCl$: M^+, 169.0658. Found: *m*/*z* 169.0658.

(*Z*)-2-(But-3-enylidene)hexanedinitrile (3as). A colorless oil, R_f 0.14 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (t, *J* = 7.7 Hz, 1H), 5.84–5.72 (m, 1H), 5.15–5.09 (m, 2H), 3.13 (t, *J* = 7.0 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 2.40 (t, *J* = 6.9 Hz, 2H), 1.93 (quint, *J* = 7.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.5, 132.9, 118.5, 117.2, 116.5, 113.0, 35.6, 32.8, 23.6, 16.2; IR (neat) 3082, 2941, 2874, 2247, 2216, 1639, 1427, 1107, 995, 922 cm^{-1}; HRMS (EI) Calcd for $C_{10}H_{12}N_2$: M^+, 160.1000. Found: *m*/*z* 160.1002.

(*Z*)-2-(3-*tert*-Butyldimethylsiloxyproply)hexa-2,5-dienenitrile (3at). A colorless oil, R_f 0.12 (hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (tt, *J* = 7.6, 1.3 Hz, 1H), 5.84–5.72 (m, 1H), 5.15–5.06 (m, 2H), 3.63 (t, *J* = 5.9 Hz, 2H), 3.11 (t, *J* = 7.0 Hz, 2H), 2.33 (td, *J* = 7.5, 0.9 Hz, 2H), 1.81–1.71 (m, 2H), 0.90 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.5, 133.6, 117.3, 116.8,

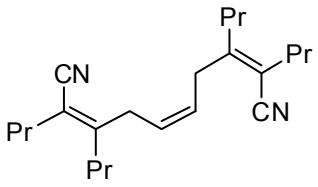
115.1, 61.3, 35.6, 31.0, 30.7, 26.1, 26.0, 18.4, –5.2; IR (neat) 2930, 2856, 2216, 1639, 1472, 1435, 1389, 1362, 1256, 1105, 968, 918, 837, 777, 664 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{27}NOSi$: $[M–(t\text{-Bu})]^+$, 208.1158. Found: *m*/*z* 208.1151.

(2*Z*,5*E*,8*Z*)-2,3-8,9,-Tetrapropyldeca-2,5-trienedinitrile (3pa). A colorless oil, R_f 0.20



(hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.51–5.46 (m, 2H), 3.10 (d, *J* = 5.1 Hz, 4H), 2.19 (t, *J* = 7.6 Hz, 4H), 2.13 (d, *J* = 7.9 Hz, 4H), 1.57 (sext, *J* = 7.5 Hz, 4H), 1.41 (sext, *J* = 7.6 Hz, 4H), 0.94 (t, *J* = 7.4 Hz, 6H), 0.92 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.0, 128.5, 118.9, 110.7, 39.2, 33.3, 31.6, 21.8, 21.2, 14.2, 13.5; IR (neat, as a mixture with **3'pa**) 2963, 2934, 2874, 2361, 2343, 2251, 2208, 1624, 1464, 1381, 1342, 1117, 1086, 972, 735 cm^{-1}. Anal. $C_{22}H_{34}N_2$: C, 80.93; H, 10.50. Found (as a mixture with **3'pa**): C, 80.95; H, 10.53.

(2*Z*,5*Z*,8*Z*)-2,3-8,9,-Tetrapropyldeca-2,5-trienedinitrile (3'pa). A colorless oil, R_f



0.20 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (t, *J* = 4.5 Hz, 2H), 3.25 (d, *J* = 5.1 Hz, 4H), 2.20 (t, *J* = 7.6 Hz, 4H), 2.15 (d, *J* = 7.9 Hz, 4H), 1.59 (sext, *J* = 7.5 Hz, 4H), 1.46 (sext, *J* = 7.6 Hz, 4H), 0.96 (t, *J* = 7.3 Hz, 6H), 0.95 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 127.7, 119.0, 110.8, 34.5, 33.5, 31.6, 21.8, 21.4, 14.3, 13.6.

Nickel/$AlMe_3$-catalyzed carbocyanation of alkynes with α-siloxyallyl cyanides. ***A general procedure.***

In a dry box, **1g** (155 mg, 1.00 mmol) and an alkyne (1.00 mmol) were added sequentially to a toluene (1.50 mL) solution of $Ni(cod)_2$ (5.6 mg, 20 μmol), $P(4\text{-}CF_3–C_6H_4)_3$ (18.7 mg, 40 μmol), and a 1.04 M solution of $AlMe_3$ in hexane (77 μL, 80 μmol). The vial was closed, taken outside the dry box, and heated at the temperature for the time both specified in Table 8. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was dissolved in THF (10 mL) and treated with a 1 M HCl aqueous solution (5.0 mL) at 0 °C. The mixture was stirred at

room temperature overnight and extracted with Et_2O. Combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash silica gel column chromatography to give the corresponding carbocyanation products in yields listed in Table 8.

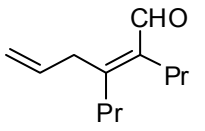
(*Z*)-2-[(Trimethylsilyl)methyl]-6-oxohex-2-enenitrile (3gr). A yellow oil, R_f 0.20 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (t, *J* = 1.0 Hz, 1H), 5.95 (td, *J* = 6.6, 1.1 Hz, 1H), 2.70–2.59 (m, 4H), 1.66 (s, 2H), 0.10 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.1, 142.0, 118.1, 113.1, 42.9, 24.7, 24.2, –1.7; IR (neat) 3443, 2955, 2989, 2214, 1728, 1416, 1250, 1169, 1140, 1113, 1090, 851, 766, 700, 644, 619 cm^{-1}; HRMS (EI) Calcd for $C_{10}H_{17}NOSi$: M^+, 195.1079. Found: *m*/*z* 195.1088.

(*Z*)-2-(2-*tert*-Butyldimethylsiloxyethyl)-6-oxohex-2-enenitrile (3gu). A yellow oil, R_f 0.18 (hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 6.24 (t, *J* = 7.4 Hz, 1H), 3.75 (t, *J* = 6.0 Hz, 2H), 2.75–2.60 (m, 4H), 2.39 (t, *J* = 6.0 Hz, 2H), 0.88 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.8, 146.9, 117.0, 113.2, 60.6, 42.5, 37.6, 25.9, 24.2, 18.4, –5.2; IR (neat) 3383, 2955, 2930, 2216, 1732, 1715, 1472, 1391, 1362, 1258, 1107, 1007, 937, 837, 779, 731, 667 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{25}NO_2Si$: $[M–(t\text{-Bu})]^+$, 210.0950. Found: *m*/*z* 210.0942.

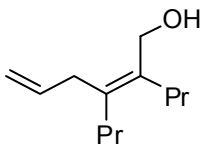
(*2Z,5E*)-6,10-Dimethyl-2-(4-oxobutylidene)undeca-5,9-dienenitrile (3gv, containing 4% of 3'gv). A pale yellow oil, R_f 0.15 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 0.04H), 9.78 (s, 0.96H), 6.15 (t, *J* = 7.4 Hz, 0.96H), 5.17 (s, 0.04H), 5.14–4.98 (m, 2H), 2.74–2.58 (m, 4H), 2.23 (s, 2H), 2.22 (s, 2H), 2.12–1.92 (m, 4H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (for **3gv**, 101 MHz, $CDCl_3$) δ 200.1, 145.0, 137.2, 131.4, 124.1, 121.6, 117.2, 115.9, 42.4, 39.6, 34.3, 26.6, 26.4, 25.7, 23.9, 17.6, 16.1; IR (neat, as a mixture with **3'gv**) 2964, 2924, 2856, 2727, 2214, 1728, 1443, 1385, 1107, 1051, 984, 893, 839 cm^{-1}. Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H,

9.71. Found (as a mixture with **3'gv**): C, 78.93; H, 9.95.

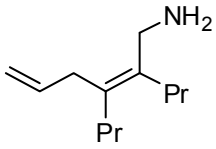
DIBAL-H reduction of 3aa. To a solution of **3aa** (53 mg, 0.30 mmol) in toluene (3.0 mL) was added a 1.5 M solution of DIBAL-H in toluene (0.50 mL, 0.75 mmol) at –78 °C, and the resulting mixture was stirred at the same temperature for 1 h. The reaction was quenched with MeOH (0.150 mL) at –78 °C and was warmed at room temperature. The mixture was diluted with CH_2Cl_2, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 25 : 1 as an eluent) to give (*Z*)-2,3-dipropylhexa-2,5-dienal (**13**, 49 mg, 90%) as a colorless oil, R_f 0.30 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 5.89–5.77 (m, 1H), 5.12–5.00 (m, 2H), 3.29 (d, *J* = 6.0 Hz, 2H), 2.28–2.18 (m, 4H), 1.49 (sext, *J* = 7.6 Hz, 2H), 1.33 (sext, *J* = 7.6 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 158.8, 137.9, 135.6, 116.7, 36.8, 34.5, 27.4, 22.8, 21.5, 14.4, 14.3; IR (neat) 2961, 2932, 2872, 1670, 1616, 1464, 1080, 991, 916 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{20}O$: M^+, 180.1514. Found: *m*/*z* 180.1523.



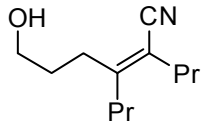
$LiAlH_4$ reduction of 13. To $LiAlH_4$ (51 mg, 1.30 mmol) suspended in THF (1.40 mL) was added a solution of **13** (49 mg, 0.27 mmol) in THF (1.50 mL) at room temperature, and the resulting mixture was stirred for 10 min before dilution with diethyl ether (4.0 mL) and quenching with H_2O (75 μL) at 0 °C. The mixture was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give (*Z*)-2,3-dipropylhexa-2,5-dien-1-ol (**13**, 45 mg, 91%) as a colorless oil, R_f 0.25 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87–5.74 (m, 1H), 5.08–4.94 (m, 2H), 4.08 (s, 2H), 2.86 (dt, *J* = 6.0, 1.6 Hz, 2H), 2.17–2.09 (m, 2H), 2.05–1.98 (m, 2H), 1.50–1.31 (m, 4H), 1.30 (br s, 1H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 135.9, 134.9, 114.7, 62.0, 36.0,34.4, 32.7, 22.3, 21.8, 14.34, 14.30; IR (neat) 3319, 2959, 2932, 2870, 1636, 1466, 1377, 1011, 910, 737 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{22}O$: M^+, 182.1671. Found: *m*/*z* 182.1666.



Reduction of 3aa with DIBAL-H followed by $NaBH_4$. To a solution of **3aa** (53 mg, 0.30 mmol) in toluene (3.0 mL) was added a 1.5 M solution of DIBAL-H in toluene (0.50 mL, 0.75 mmol) at –78 °C, and the resulting mixture was stirred at –78 °C for 1 h. The reaction was quenched with MeOH (0.100 mL) at –78 °C and was warmed at room temperature. The mixture was diluted with CH_2Cl_2, filtered through a Celite pad, and concentrated *in vacuo*. To a solution of the residue in MeOH (1.00 mL) was added $NaBH_4$ (57 mg, 1.50 mmol) portionwise at 0 °C, and the resulting mixture was stirred at 0 °C for 40 min. The reaction was quenched with a 1.0 M HCl aqueous solution at 0 °C, and the resulting mixture was extracted with diethyl ether for three times. The combined organic layers were washed with a saturated $NaHCO_3$ aqueous solution and brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give (*Z*)-2,3-dipropylhexa-2,5-dien-1-amine (**15**, 21 mg, 38%) as a colorless oil, R_f 0.15 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.82–5.68 (m, 1H), 5.05–4.89 (m, 2H), 3.09 (s, 2H), 2.81 (d, *J* = 6.0 Hz, 2H), 2.13–1.94 (m, 4H), 1.46–1.30 (m, 4H), 1.25 (br s, 1H), 0.91 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 134.1, 133.7, 114.5, 49.4, 36.0, 34.2, 33.1, 22.4, 22.0, 14.4; IR (neat) 3078, 2957, 2930, 2870, 1825, 1740, 1636, 1464, 1456, 1377, 1259, 1092, 993, 908, 743 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{22}N$: $[M–H]^+$, 180.1763. Found: *m*/*z* 180.1758.

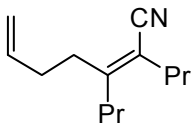


$NaBH_4$ reduction of 3ga. To a solution of **3ga** (19.3 mg, 0.100 mmol) in MeOH (0.33 mL) was added $NaBH_4$ (11.3 mg, 0.30 mmol) portionwise at 0 °C, and the resulting mixture was stirred at the same temperature for 10 min. The reaction was quenched with a 1.0 M HCl aqueous solution at 0 °C, and the resulting mixture was extracted with diethyl ether for 3 times. The combined organic layers were washed with a saturated $NaHCO_3$ aqueous solution and brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give (*Z*)-6-hydroxy-2,3-dipropylhex-2-enenitrile (**16**, 15.8 mg, 81%) as a colorless oil, R_f 0.13 (hexane–ethyl acetate = 3 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.67 (t, *J* = 6.4 Hz, 2H), 2.46 (t, *J* = 7.8 Hz, 2H), 2.22–2.10 (m, 4H), 1.79–1.65 (m, 3H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.43 (sext, *J* = 7.6

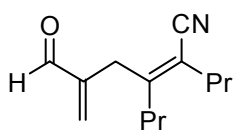


Hz, 2H), 0.933 (t, J = 7.5 Hz, 3H), 0.929 (t, J = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 119.4, 110.4, 62.0, 33.4, 32.2, 31.4, 31.2, 21.7, 21.3, 14.1, 13.4; IR (neat) 3439, 2961, 2934, 2874, 2208, 1622, 1458, 1061 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{21}NO$: M^+, 195.1623. Found: *m*/*z* 195.1615.

Carbonyl methylenation of 3ga with $CH_2(ZnI)_2$.[14] To a solution of **3ga** (0.190 g, 0.100 mmol) in THF (0.50 mL) was added a 0.40 M solution of $CH_2(ZnI)_2$ in THF (1.00 mL, 0.40 mmol) at room temperature, and the resulting mixture was stirred for 0.5 h. The reaction was quenched with MeOH at 0 °C, and a saturated NH_4Cl aqueous solution was added to the mixture. The resulting mixture was extracted with diethyl ether for 3 times, and the combined organic layers were washed with a saturated NH_4Cl aqueous solution and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel to give (*Z*)-2,3-dipropylhepta-2,5-dienenitrile (**17**, 13.7 mg, 72%) and recovered **3ga** (3.6 mg, 19%). **17** is a colorless oil, R_f 0.38 (hexane–ethyl acetate = 15 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88–5.74 (m, 1H), 5.09–4.95 (m, 2H), 2.48 (t, J = 7.7 Hz, 2H), 2.28–2.08 (m, 6H), 1.56 (sext, J = 7.4Hz, 2H), 1.43 (sext, J = 7.6 Hz, 2H), 0.94 (t, J = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 137.0, 119.2, 115.6, 110.6, 35.3, 33.3, 32.5, 31.5, 21.7, 21.3, 14.1, 13.4; IR (neat) 2963, 2934, 2874, 2208, 1641, 1622, 1456, 1381, 995, 912 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{21}N$: M^+, 191.1674. Found: *m*/*z* 191.1683.



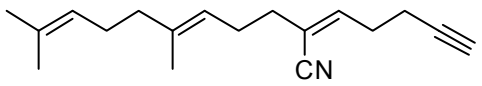
***α*−Methylenation of 3ga.**[13] To a mixture of **3ga** (58 mg, 0.30 mmol), a 37% formaldehyde aqueous solution (37 mg, 0.45 mmol), and 2-propanol (30 μL) were added propionic acid (2.2 mg, 30 μmol) and pyrrolidine (2.1 mg, 30 μmol). The resulting mixture was stirred at 45 °C for 24 h, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give (*Z*)-5-methylene-6-oxo-2,3-dipropylhex-2-enenitrile (**18**, 51 mg, 83%) as a colorless oil, R_f 0.23 (hexane–ethyl acetate = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 6.27 (t, J = 1.5 Hz, 1H), 6.14 (t, J = 1.0 Hz, 1H), 3.34 (s, 2H), 2.23 (t, J = 7.6 Hz, 2H), 2.06 (t, J = 7.9 Hz, 2H), 1.60 (sext, J = 7.5 Hz, 2H), 1.40 (sext, J = 7.6 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H), 0.90 (t, J = 7.3 Hz,



3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 155.7, 146.2, 135.5, 119.0, 113.1, 33.5, 33.3, 31.5, 21.7, 21.3, 14.1, 13.5; IR (neat) 2963, 2934, 2874, 2208, 1693, 1626, 1466, 1437, 1344, 1242, 1111, 1086, 959, 735 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{19}NO$: M^+, 205.1467. Found: *m*/*z* 205.1469.

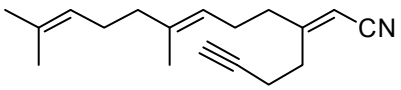
Homologation of 3gv. To a solution of a mixure of **3gv** and **3'gv** (245 mg, 1.00 mmol) and K_2CO_3 (0.62 g, 4.5 mmol) in MeOH (20 mL) was added dimethyl 1-diazo-2-oxopropylphosphonate (**21**, 0.58 g, 3.0 mmol) dropwise at room temperature, and the resulting mixture was stirred at room temperature for 22 h before quenching with H_2O (10 mL). The resulting mixture was extracted with diethyl ether for 3 times. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and purified by flash chromatography on silica gel (hexane–ethyl acetate = 30 : 1 as an eluent) to give (2*Z*,5*E*)-6,10-dimethyl-2-(pent-4-ynylidene)undeca-5,9-dienenitrile (**22**, 156 mg, 61%) and its regioisomer (2*Z*,6*E*)-3-(but-3-yn-1-yl)-7,11-dimethyldodeca-2,6,10-trienenitrile (**22'**, 8.5 mg, 3%).

(2*Z*,5*E*)-6,10-dimethyl-2-(pent-4-ynylidene)undeca-5,9-dienenitrile (22). A pale



yellow oil, R_f 0.25 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.22 (t, *J* = 7.5 Hz, 1H), 5.15–4.99 (m, 2H), 2.56 (q, *J* = 7.1 Hz, 2H), 2.33 (td, *J* = 7.0, 2.6 Hz, 2H), 2.25 (s, 4H), 2.11–1.94 (m, 5H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 137.1, 131.5, 124.1, 121.7, 117.4, 115.9, 82.3, 69.7, 39.6, 34.4, 30.1, 26.6, 26.4, 25.7, 17.9, 17.7, 16.1; IR (neat) 3298, 2964, 2918, 2856, 2218, 1437, 1377, 1327, 1107, 1088, 986, 891, 833, 638 cm^{-1}. Anal. Calcd for $C_{18}H_{25}N$: C, 84.65; H, 9.87. Found: C, 84.47; H, 9.97.

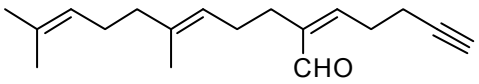
(2*Z*,6*E*)-3-(But-3-yn-1-yl)-7,11-dimethyldodeca-2,6,10-trienenitrile (22'). A pale



yellow oil, R_f 0.10 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.19 (s, 1H), 5.12–4.98 (m, 2H), 2.63 (t, *J* = 7.3 Hz, 2H), 2.43 (td, *J* = 7.2, 2.6 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H),

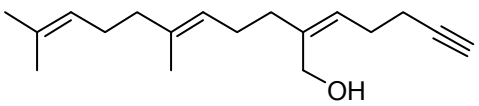
2.17 (q, J = 7.1 Hz, 2H), 2.11–1.94 (m, 4H), 2.02 (t, J = 2.7 Hz, 1H), 1.68 (s, 3H), 1.60 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 137.0, 131.6, 124.0, 121.9, 116.8, 96.5, 82.0, 69.9, 39.6, 35.9, 33.3, 26.5, 25.7, 25.5, 17.7, 17.2, 16.1; IR (neat) 3298, 2695, 2924, 2857, 2218, 1719, 1626, 1451, 1377, 1325, 1109, 1090, 984, 827, 640 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{25}N$: M^+, 255.1987. Found: *m*/*z* 255.1984.

DIBAL-H reduction of 22. To a solution of **22** (0.51 g, 2.0 mmol) in toluene (20 mL) was added a 1.5 M solution of DIBAL-H in toluene (3.3 mL, 5.0 mmol) at –78 °C, and the resulting mixture was stirred at the same temperature for 1.5 h. The reaction was quenched with MeOH (1.00 mL) at –78 °C and was warmed at room temperature. The mixture was diluted with CH_2Cl_2, filtered through a Celite pad, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate = 30 : 1 as an eluent) to give (2*Z*,5*E*)-6,10-dimethyll-2-(pent-4-ynylidene)undeca-5,9-dienenitrile (**23**, 0.48 g, 93%)



as a colorless oil, R_f 0.20 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.1 (s, 1H), 6.47 (t, J = 8.2 Hz, 1H), 5.14–5.04 (m, 2H), 2.78 (q, J = 7.3 Hz, 2H), 2.38 (td, J = 7.0, 2.6 Hz, 2H), 2.23 (t, J = 7.5, 2H), 2.15–1.92 (m, 6H), 2.00 (t, J = 2.6, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.5, 145.8, 140.9, 135.8, 131.2, 124.2, 123.1, 82.4, 70.0, 39.8, 30.5, 27.1, 26.8, 25.8, 25.5, 18.9, 17.8, 16.2; IR (neat) 3306, 2965, 2918, 2855, 1678, 1435, 1375, 1366, 1260, 1148, 1107, 1092, 1028, 806, 638 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{26}O$: M^+, 258.1984. Found: *m*/*z* 258.1973.

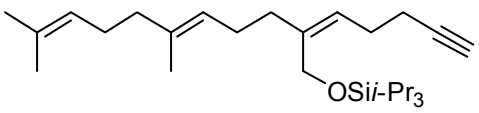
$LiAlH_4$ reduction of 23. To a suspension of $LiAlH_4$ (0.35 g, 9.3 mmol) in THF (9.3 mL) was added a solution of **23** (0.48 g, 1.86 mmol) in THF (1.50 mL) at 0 °C, and the resulting mixture was stirred for 20 min before dilution with diethyl ether (20 mL) and quenching with H_2O (0.50 mL) at 0 °C. The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column



chromatography on silica gel to give (2*Z*,5*E*)-6,10-dimethyl-2-(pent-4-ynylidene)unde

ca-5,9-dien-1-ol (**24**, 0.46 mg, 95%) as a colorless oil, R_f 0.20 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (t, *J* = 7.3 Hz, 1H), 5.18–5.04 (m, 2H), 4.13 (s, 2H), 2.37–1.92 (m, 13H), 1.68 (s, 3H), 1.60 (s, 6H), 1.33 (br s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 135.5, 131.3, 126.4, 124.3, 123.8, 84.4, 68.7, 60.1, 39.7, 35.3, 26.8, 26.7, 26.6, 25.7, 19.0, 17.7, 16.1; IR (neat) 3308, 2965, 2924, 2857, 2118, 1668, 1445, 1377, 1327, 1240, 1142, 1109, 1005, 837, 633 cm^{-1}. Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.83; H, 11.02.

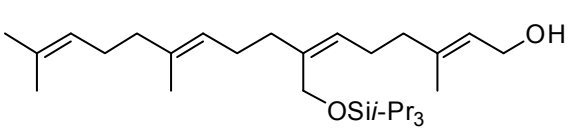
Silylation of 24. To a solution of **24** (26.0 mg, 0.100 mmol) and imidazole (35 mg, 0.51 mmol) in DMF (0.33 mL) was added triisopropylsilyl chloride (50 mg, 0.25 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 3 h before quenching with H_2O. The resulting mixture was extracted with diethyl ether. The combined organic layers were washed with water and brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and purified by flash chromatography on silica gel to give (5*Z*,9*E*)-10,14-dimethyl-6-(triisopropylsiloxymethyl)-pentadeca-5,9,13-trien-1-yne



(**25**, 42 mg, quant) as A colorless oil, R_f 0.70 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (t, *J* = 7.0 Hz, 1H), 5.18–4.95 (m, 2H), 4.27 (s, 2H), 2.33–1.93 (m, 12H), 1.95 (t, *J* = 2.6 Hz, 1H), 1.69 (s, 3H), 1.61 (s, 6H), 1.18–1.04 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.3, 134.8, 131.1, 124.3, 124.2, 123.6, 84.2, 68.4, 60.8, 39.8, 34.7, 26.89, 26.87, 26.85, 25.8, 19.3, 18.2, 17.8, 16.2, 12.2; IR (neat) 3314, 2961, 2942, 2866, 2120, 1462, 1383, 1248, 1088, 1067, 1013, 995, 882, 808, 683, 635 cm^{-1}. Anal. Calcd for $C_{27}H_{48}OSi$: C, 77.81; H, 11.61. Found: C, 78.07; H, 11.42.

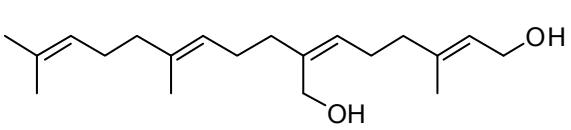
Methylalmination of 25 followed by reaction with paraformaldehyde.[19b] To a oven dried vial were added *rac*-ethylenebis(indenyl)zirconocene dichloride **28**[20] (2.1 mg, 5.0 μmol) and then a 1.8 M solution of $AlMe_3$ in toluene (83 μL, 0.150 mmol) dropwise at room temperature. Under stirring at room temperature, a 7.5% w/w solution of MAO in toluene (4.5 μL, 5.0 μmol) was added. To the **25** (42 mg, 0.100 mmol) mixture was added, and the resulting homogeneous golden orange solution was stirred at room

temperature for 48 h. All the volatile materials were completely removed under reduced pressure, and the residue was dissolved in THF (200 μL). To this solution were added a 1.6 M solution of *n*-BuLi in hexane (69 μL, 0.110 mmol) and paraformaldehyde (9.0 mg, 0.30 mmol) successively at room temperature. After 1.5 h, the resulting mixture was filtered through a silica gel pad, and the filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give



(2*E*,6*Z*,10*E*)-3,11,15-trimethyl-7-(triisopropylsiloxymethyl)hexadeca-2,6,10,14-tetraen-1-ol (**26**, 27 mg, 59%) as a pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.41 (t, *J* = 7.0 Hz, 1H), 5.18 (t, *J* = 7.0 Hz, 1H), 5.17–5.04 (m, 2H), 4.25 (s, 2H), 4.15 (d, *J* = 7.0 Hz, 2H), 2.20–1.92 (m, 12H), 1.68 (s, 6H), 1.61 (s, 6H), 1.18–1.00 (m, 21H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 139.0, 134.7, 131.1, 125.0, 124.3, 123.5, 60.7, 59.4, 39.9, 39.8, 34.6, 27.0, 26.9, 26.0, 25.8, 18.2, 17.8, 16.4, 16.2, 12.2; IR (neat) 3337, 2942, 2866, 1458, 1381, 1086, 1065, 1013, 995, 882, 812, 681, 660 cm^{-1}; HRMS (EI) Calcd for $C_{26}H_{45}O_2Si$: $[M–(i\text{-}Pr + H_2)]^+$, 417.3189. Found: *m*/*z* 417.3188.

Plaunotol 27.[17g] To a solution of **26** (58 mg, 0.124 mmol) in THF (1.25 mL) was added a 1.0 M solution of TBAF in THF (0.62 mL, 0.62 mmol) at room temperature, and the resulting mixture was stirred at room temperature for 12 h. The reaction was quenched with a saturated NH_4Cl aqueous solution, and the resulting mixture was extracted with diethyl ether. The combined organic layers were washed with a saturated NH_4Cl aqueous solution and brine, dried over anhydrous $MgSO_4$, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give plaunotol (**27**, 34 mg, 89%) as a colorless oil, R_f 0.15 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (td, *J* = 7.0, 1.2 Hz, 1H), 5.28 (t, *J* = 7.5 Hz, 1H), 5.17–5.00 (m, 2H), 4.14 (d, *J* = 7.1 Hz, 2H), 4.10 (s, 2H), 2.22 (q, *J* = 7.3 Hz, 2H), 2.19–2.08 (m, 4H), 2.06 (t, *J* = 7.4 Hz, 2H), 2.02–1.94 (m, 2H), 1.70 (s, 3H), 1.69 (s, 6H), 1.61 (s, 6H), 1.55 (br s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 138.7, 135.3, 131.2, 127.6, 124.2, 123.91, 123.86, 60.1, 59.2, 39.8,



39.4, 35.1, 27.0, 26.8, 26.0, 25.8, 17.8, 16.6, 16.2; IR (neat) 3331, 2995, 2922, 2857, 1667, 1445, 1381, 1238, 1105, 1005, 837, 743 cm^{-1}. The spectra data above were identical to those reported previously.

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Chapter 3

Alkynylcyanation of Alkynes and Dienes Catalyzed by Nickel

Alkynyl cyanides are found to add across alkynes and 1,2-dienes in the presence of a catalyst prepared in situ from $Ni(cod)_2$, Xantphos, and BPh_3. A range of functionalized conjugated *cis*-enynes are obtained with high regioselectivity. The addition reaction across norbornadiene proceeds in the absence of BPh_3 to give *exo*-*cis* adducts exclusively. A stoichiometric reaction of an alkynyl cyanide, $Ni(cod)_2$, Xantphos, and BPh_3 gave *trans*-(xantphos)Ni($CNBPh_3$)(C≡C$SiMe_2$*t*-Bu) (**4**), which was suggested to be a plausible reaction intermediate of the alkynylcyanation reaction.

Introduction

As discussed in Chapter1, nickel or nickel/Lewis acid-catalyzed addition of nitriles across unsaturated bonds, namely carbocyanation reactions,[1] has provided a new transformations that proceed through oxidative addition of C–CN bonds to nickel(0).[2,3] The scope of nitriles for the carbocyanation covers aryl, alkenyl, and alkyl cyanides. Alkynyl cyanides are readily available from terminal alkynes and cyano phenolate[4a] and have also been demonstrated to undergo the oxidative addition to platinum(0) through the activation of C(sp)–CN bonds.[5] The author therefore has anticipated that the carbocyanation reaction using alkynyl cyanides would be achieved by transition metal catalysts to allow direct installation of alkynyl and cyano groups in a single operation. Described in this Chapter is nickel/BPh_3-catalyzed regio- and stereoselective alkynylcyanation of alkynes and 1,2-dienes to afford highly functionalized conjugated enynes.[6] Also demonstrated is that alkynyl cyanides add across norbornadiene stereoselectively. A mechanism for the alkynylcyanation reaction is discussed based on both stoichiometric and catalytic reactions using structurally characterized *trans*-(xantphos)Ni($CNBPh_3$)(C≡C$SiMe_2$*t*-Bu), which is obtained by the oxidative addition of an alkynyl cyanide to nickel/xantphos in the presence of BPh_3.

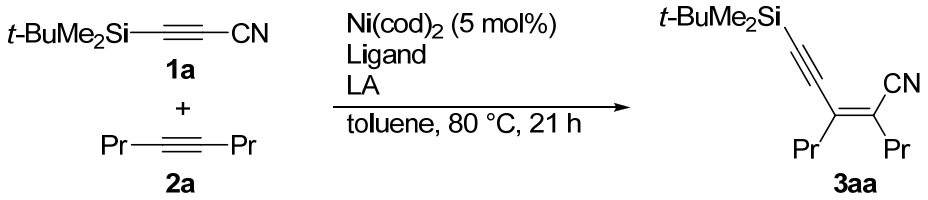
Results and discussion

Nickel/BPh_3-catalyzed Alkynylcyanation of Alkynes

The author first examined the reaction of 3-*tert*-butyldimethylsilyl-2-propynenitrile (**1a**) with 4-octyne (**2a**) in the presence of a catalytic amount of $Ni(cod)_2$ with various ligands and Lewis acid (LA) catalysts (Table 1). All the phosphorous ligands examined including monodentate or bidentate gave at most only a detectable amount of expected alkynylcyanation product **3aa**, whereas use of Xantphos significantly effective to obtain **3aa** in a moderate yield (entry 14). The *cis*-addition was unambiguously confirmed by nOe experiments of ^{1}H NMR after reduction of the cyano group to formyl (*vide infra*). He then examined the effects of Lewis acid cocatalysts and found that triarylboranes such as BPh_3 and $B(C_6F_5)_3$ were highly effective (entries 15 and 16), while aluminum-based Lewis acid catalysts, which are effective for arylcyanation reaction,[1d] gave lower yields of **3aa** (entries 17 and 18). A high catalyst turnover was attained even in the presence of 1 mol% of the nickel catalyst and 3 mol% of BPh_3 to give **3aa** in 95%

yield after isolation by flash column chromatography on silica gel (entry 19). Use of BPh_3 in less than 3 mol% resulted in low yield of **3aa** proportionally (entries 20 and 21). Polar solvents like 1,4-dioxane and DMF were less effective (entries 22 and 23).

Table 1. Alkynylcyanation of 4-octyne (**2a**) using alkynyl cyanide **1a**.[a]



Entry	Ligand (mol%)	Lewis acid (mol%)	Solvent	Yield (%)[b]
1	PMe_3 (10)	none	toluene	0
2	PCy_3 (10)	none	toluene	0
3	P*t*-Bu_3 (10)	none	toluene	6
4	PMe_2Ph (10)	none	toluene	5
5	$PMePh_2$ (10)	none	toluene	9
6	PPh_3 (10)	none	toluene	5
7	P(4-MeO–C_6H_4)$_3$ (10)	none	toluene	4
8	P(4-CF_3–C_6H_4)$_3$ (10)	none	toluene	14
9	dppb (5)	none	toluene	0
10	dpppent (5)	none	toluene	2
11	dpphex (5)	none	toluene	6
12	dppf (5)	none	toluene	0
13	DPEphos (5)	none	toluene	5
14	Xantphos (5)	none	toluene	62
15	Xantphos (5)	BPh_3 (15)	toluene	100
16	Xantphos (5)	$B(C_6F_5)_3$ (15)	toluene	92
17	Xantphos (5)	$AlMe_3$ (15)	toluene	15
18	Xantphos (5)	$AlMe_2Cl$ (15)	toluene	39
19[c]	Xantphos (1)	BPh_3 (3)	toluene	100 (95)[d]
20[c]	Xantphos (1)	BPh_3 (2)	toluene	59
21[c]	Xantphos (1)	BPh_3 (1)	toluene	23
22[c]	Xantphos (1)	BPh_3 (3)	DMF	0
23[c]	Xantphos (1)	BPh_3 (3)	dioxane	21

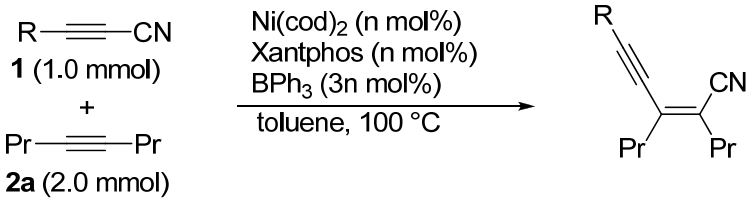
[a] All the reaction was carried out using **1a** (0.20 mmol), **2a** (0.20 mmol), $Ni(cod)_2$ (5.0 mol%), a ligand, and a Lewis acid catalyst in toluene (0.3 mL). [b] Estimated by GC using tetradecane as an internal standard. [c] $Ni(cod)_2$ (1.00 mol%) was used. [d] Isolated yield obtained with a 1.00 mmol scale.

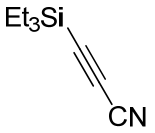
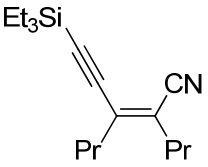
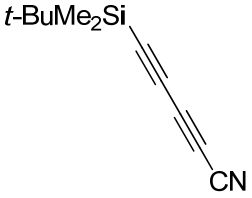
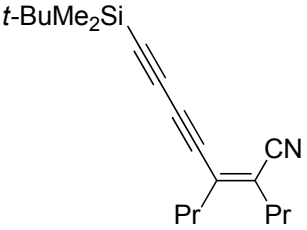
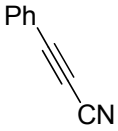
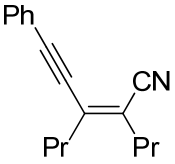
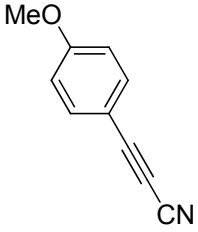
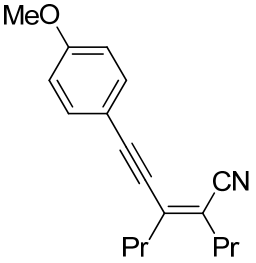
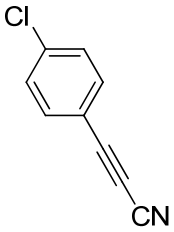
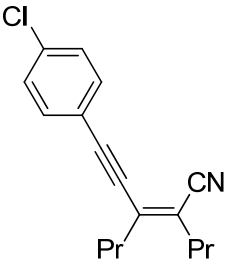
With the optimized conditions in hand, the author next studied scope of alkynyl cyanides with **2a** as an alkyne substrate (Table 2). Triethylsilyl variant **1b** also added across **2a** in an excellent yield (entry 1). Using diynyl cyanide **1c** as a nitrile substrate, conjugated endiyne **3ca** was successfully obtained in 72% yield (entry 2). Reactions of

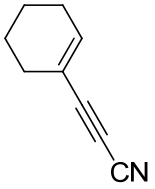
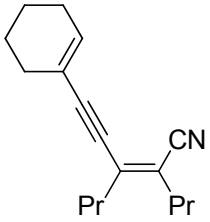
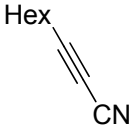
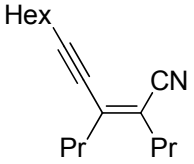
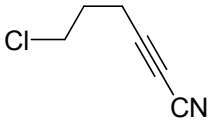
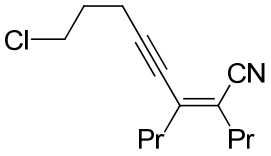
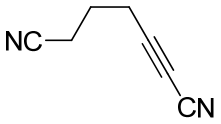
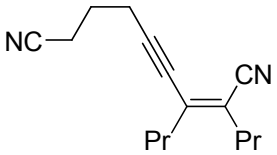
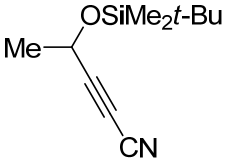
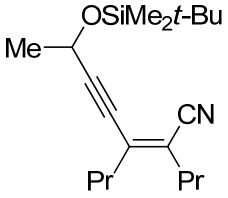
aryl-, alkenyl-, and alkylethynyl cyanides with two molar equivalents of **2a** also gave the corresponding conjugated enynes in modest to good yields in the presence of 10 mol% of the nickel catalyst and 30 mol% of BPh_3 at higher reaction temperatures (entries 3–10).[7] It is noteworthy that a C(sp)–CN bond is preferentially activated over C–Cl and C(sp^3)–CN bonds, which may also oxidatively add to nickel(0) (entries 5, 8, and 9). A conjugated dienyne structure was obtained with 3-cyclohexenylprop-1-ynenitrile (**1g**) (entry 6).

Scope of alkynes was next investigated with **1a** (Table 3). All the reactions proceeded through exclusive *cis*-addition of the alkynyl cyanide as confirmed by nOe experiments of ^1H NMR, ^1H–^1H couplings, and/or HMBC experiments of the corresponding aldehydes **4** (*vide infra*). Addition of **1a** across 1-phenyl-1-propyne (**2b**) gave the corresponding adducts (**3ab** and **3'ab**) in good yields but with poor regioselectivitiy (entry 1). An isomer having the phenyl group at the cyano-substituted carbon was obtained as a major product. Alkynes having sterically biased substituents such as 4-methyl-2-pentyne (**2c**) and 2-butyn-1-al diethyl acetal (**2d**) showed regioselectivities opposite to arylcyanation of alkynes,[1a,b] giving adducts with a bulkier substituent at the alkynyl substituted carbon (entries 2 and 3). The addition of **1h** across **2d** showed higher regioselectivity, and **3'hd** was isolated as a sole product albeit in a modest yield (entry 4). Terminal alkynes also participated in the reaction with **1a** to give conjugated enynes having a substituent at the cyano-substituted carbon with fair to excellent regioselectivities (entries 5–9). Functional groups like chloro, alkanenitrile, and ester were tolerated (entries 6–8).

Table 2. Nickel/BPh_3-catalyzed alkynylcyanation of 4-octyne (**2a**).[a]



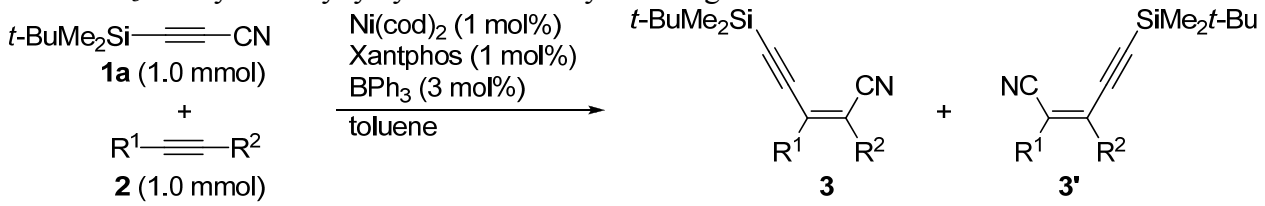
Entry	Alkynyl cyanide	n	Temp (°C)	Time (h)	Product	Yield (%)[b]
1[c]	 **1b**	1	80	24	 **3ba**	95
2[c]	 **1c**	3	80	21	 **3ca**	72
3	 **1d**	10	100	3	 **3da**	69
4	 **1e**	10	100	2	 **3ea**	68
5	 **1f**	10	100	3	 **3fa**	45

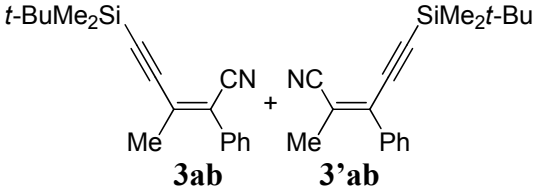
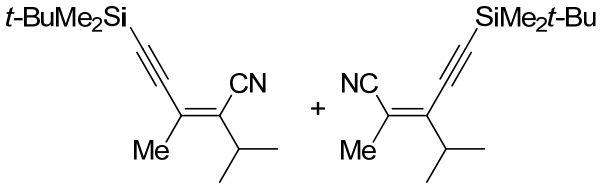
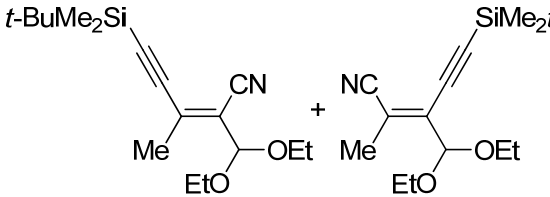
6	 **1g**	10	80	2	 **3ga**	67
7	 **1h**	10	100	3	 **3ha**	72
8	 **1i**	10	100	3	 **3ia**	54
9	 **1j**	10	100	4	 **3ja**	35
10	 **1k**	10	100	1	 **3ka**	47

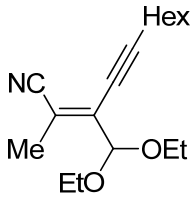
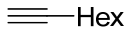
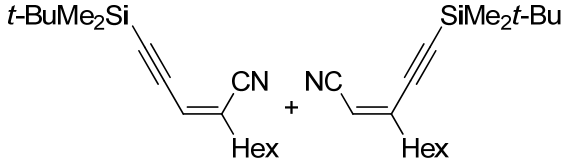
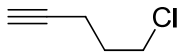
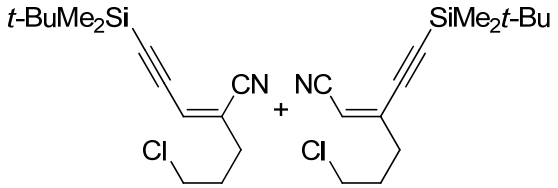
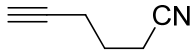
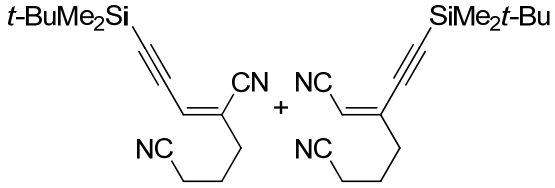
[a] Reactions were carried out using an alkynyl cyanide (1.00 mmol), **2a** (2.0 mmol), $Ni(cod)_2$ (1.00–10.0 mol%), Xantphos (1.00–10.0 mol%), and BPh_3 (3.0–30 mol%) in toluene (1.50 mL). [b] Isolated yield. [c] 1.00 mmol of **2a** was used.

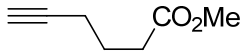
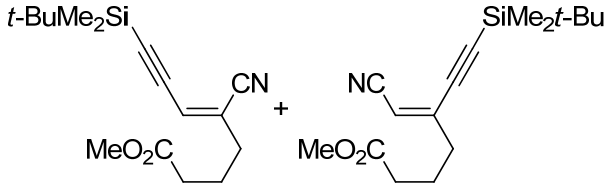
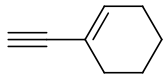
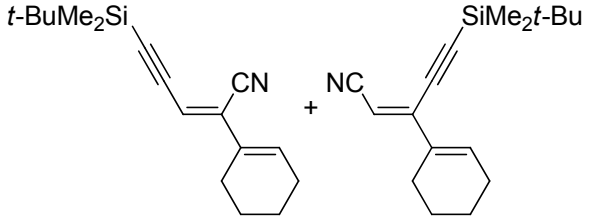
The addition reaction across aryl-substituted alkynes gave *trans*-adducts in varying amounts (Table 4). Diaryl acetylene **2j** gave *trans*-adduct (*E*)-**3aj** as a major product, the stereochemistry of which was determined by X-ray crystallographic analysis (Figure 1). Electron-poor and neutral arylacetylenes **2k** and **2m** showed moderate to good regioselectivities similar to those observed with other terminal alkynes and gave only a small amount of *trans*-adducts and regioisomers (entries 2 and 4), whereas electron-rich one **2l** reacted regioselectively but gave *trans*-adducts in a larger amount (entry 3).

Table 3. Nickel/BPh_3-catalyzed alkynylcyanation of alkynes using **1a**.[a]



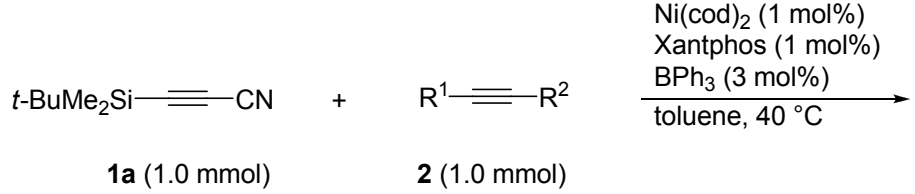
Entry	**2**	Temp (°C)	Time (h)	Products	Yield (%)[b] (**3**:**3'**)[c]
1	Me—≡—Ph **2b**	80	56	 **3ab** **3'ab**	94 (60:40)
2	Me— **2c**	80	49	 **3ac** **3'ac**	82 (22:78)
3	Me— OEt OEt **2d**	80	39	 **3ad** **3'ad**	84 (13:87)

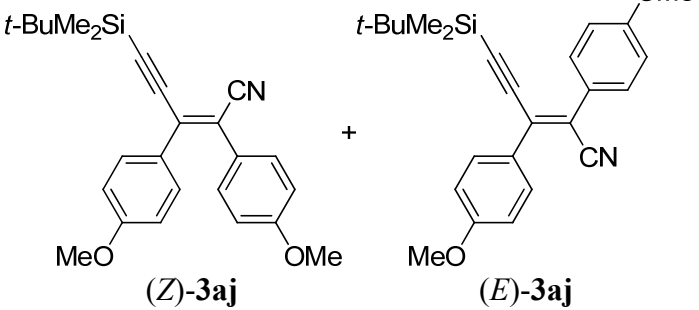
4[d]	**2d**	100	12	 **3'hd**	47 (5:>95)
5	 **2e**	40	15	 **3ae** **3'ae**	96 (83:13)
6	 **2f**	40	15	 **3af** **3'af**	79 (82:18)[e]
7	 **2g**	40	15	 **3ag** **3'ag**	99 (88:12)

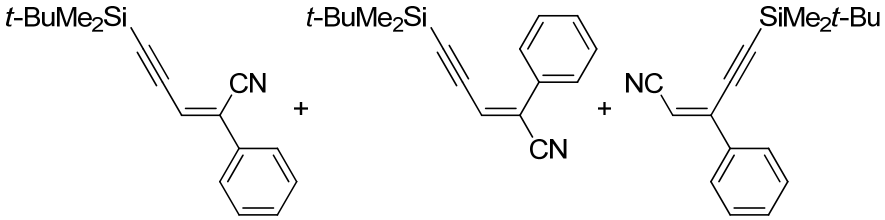
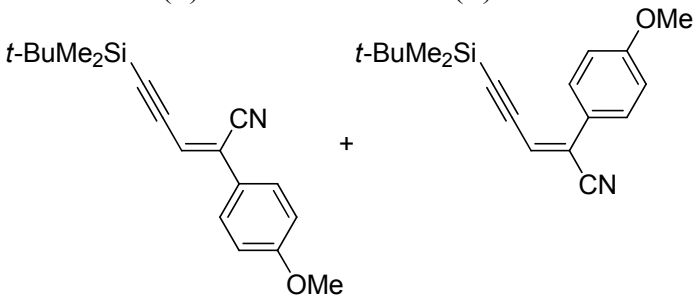
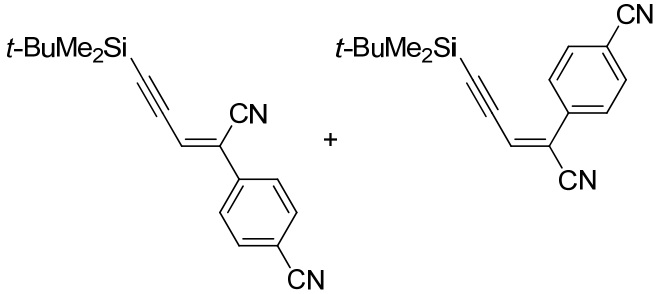
8[f]	 **2h**	40	17	 **3ah** **3'ah**	93 (87:13)
9	 **2i**	40	15	 **3ai** **3'ai**	86 (95:5)

[a] All the experiment was carried out using **1a** (1.00 mmol), an alkyne (1.00 mmol), $Ni(cod)_2$ (1.00 mol%), Xantphos (1.00 mol%), and BPh_3 (3.0 mol%) in toluene (1.50 mL). [b] Isolated yield. [c] Estimated by ^1H NMR analysis of an isolated product. [d] The reaction was carried out using $Ni(cod)_2$ (10.0 mmol%), Xantphos (10.0 mol%), and BPh_3 (30 mol%). [e] Calculated based on yields of isolated products. [f] The amount of **2h** used was 1.10 mmol.

Table 4. Nickel/BPh_3-catalyzed alkynylcyanation of aryl-substituted alkynes using **1a**.[a]



Entry	**2**	Time (h)	Products	Yield (%)[b] [(*Z*)-**3**:(*E*)-**3**:(*Z*)-**3'**][c]
1[d]	**2j**	48		100 (11:89)

2	**2k**	36	 (*Z*)-**3ak** (*E*)-**3ak** **3'ak**	97 (77:11:12)
3	**2l**	48	 (*Z*)-**3al** (*E*)-**3al**	93 (75:25)
4	**2m**	17	 (*Z*)-**3am** (*E*)-**3am**	96 (98:2)

[a] All the reaction was carried out using **1a** (1.00 mmol), an alkyne (1.00 mmol), $Ni(cod)_2$ (1.00 mol%), Xantphos (1.00 mol%), and BPh_3 (3.0 mol%) in toluene (1.50 mL). [b] Isolated yield. [c] Estimated by ^1H NMR analysis of an isolated product. [d] Reaction was carried out using **1a** (1.00 mmol), **2j** (1.00 mmol), $Ni(cod)_2$ (3.0 mmol%), Xantphos (3.0 mol%), and BPh_3 (9.0 mol%) in toluene (1.50 mL) at 80 °C.

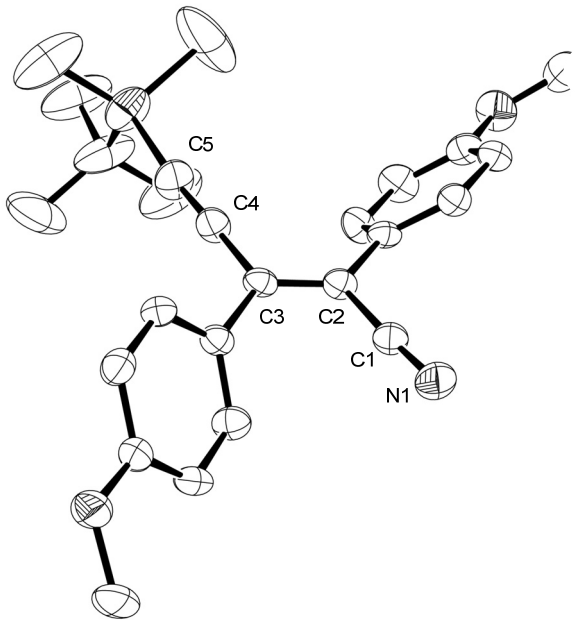
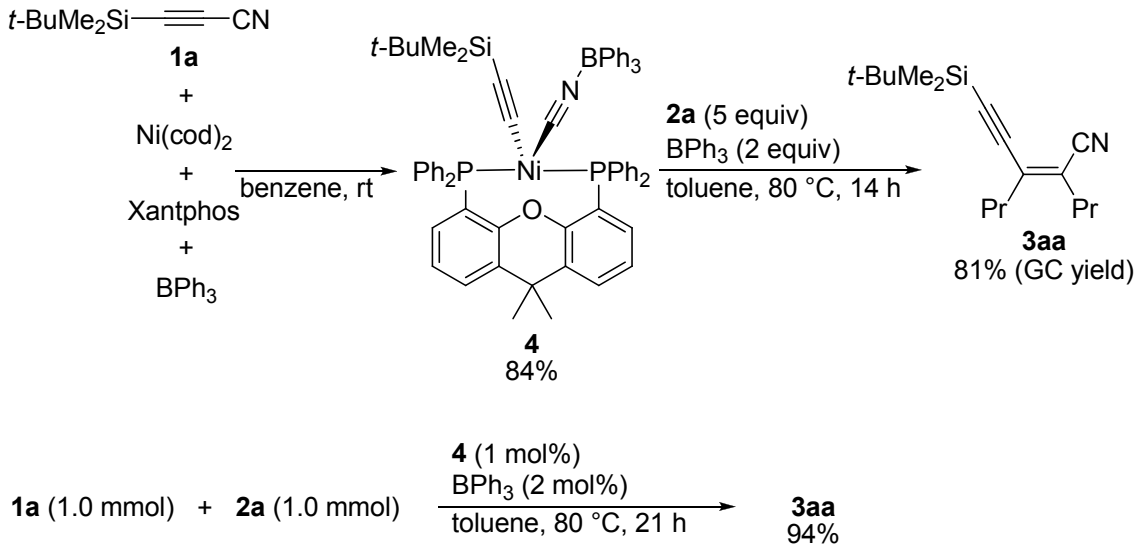


Figure 1. ORTEP drawing of (*E*)-**3aj**.

To gain a mechanistic insight, the author examined a stoichiometric reaction. Upon mixing stoichiometric amounts of **1a**, $Ni(cod)_2$, Xantphos, and BPh_3 in benzene, the initially heterogeneous reaction mixture immediately turned to a homogeneous solution at room temperature. After evaporation of benzene *in vacuo* followed by washing the resulting precipitates with hexane, *trans*-(xantphos)Ni($CNBPh_3$)(C≡C$SiMe_2$*t*-Bu) (**4**) was obtained as a brown powder in 84% yield (Scheme 1). Dark red single crystals suitable for X-ray crystallographic analysis were obtained by recrystallization from hexane and dichloromethane. The X-ray structure of **4** shown in Figure 2 clearly indicates the *trans* geometry with a cyano ligand coordinating to BPh_3. Treatment of **4** with **2a** (5.0 equiv) and BPh_3 (2.0 equiv) in toluene at 80 °C for 14 h gave alkynylcyanation product **3aa** in 81% yield as estimated by GC. Reaction below 50 °C showed no appreciable change in both **4** and **2a**: thus, the coordination of **2a** to the nickel center appears to be a plausible rate-determining step. Moreover, the reaction of **1a** (1.00 mmol) with **2a** (1.00 mmol) in the presence of a catalytic amount of **4** (1 mol%) and BPh_3 (2 mol%) in toluene at 80 °C for 21 h also gave **3aa** in 94% yield, clearly indicating that **4** should be a plausible reaction intermediate for the present alkynylcyanation reaction.



Scheme 1. Synthesis and reactions of *trans*-(xantphos)Ni(CNBPh$_3$)(C≡CSiMe$_2$*t*-Bu) (**4**).

On the other hand, the reaction of **4** with 1-octyne (**2e**, 5.0 equiv) in C_6D_6 proceeded at room temperature, and **4** was completely consumed after 6 h to give a complex which showed signals for ^{31}P NMR at 23.7 (d, J = 22.3 Hz) ppm and 23.2 (d, J = 22.3 Hz) ppm, and alkynylcyanation products **3ae** and **3'ae** were also observed in ^{1}H NMR in 79% and 14% yields as estimated by GC, respectively (Scheme 2). The new nickel complex observed was assigned to be *cis*-(xantphos)Ni(1-octyne) (**5**) based on the same set of peaks observed in the reaction of Ni(cod)$_2$, Xantphos, and **2e** (5.0 equiv). These data indicate that coordination and migratory insertion followed by reductive elimination are very rapid with terminal alkynes as has also been anticipated by the difference of the reaction temperature (80 °C vs. 40 °C, Table 3).

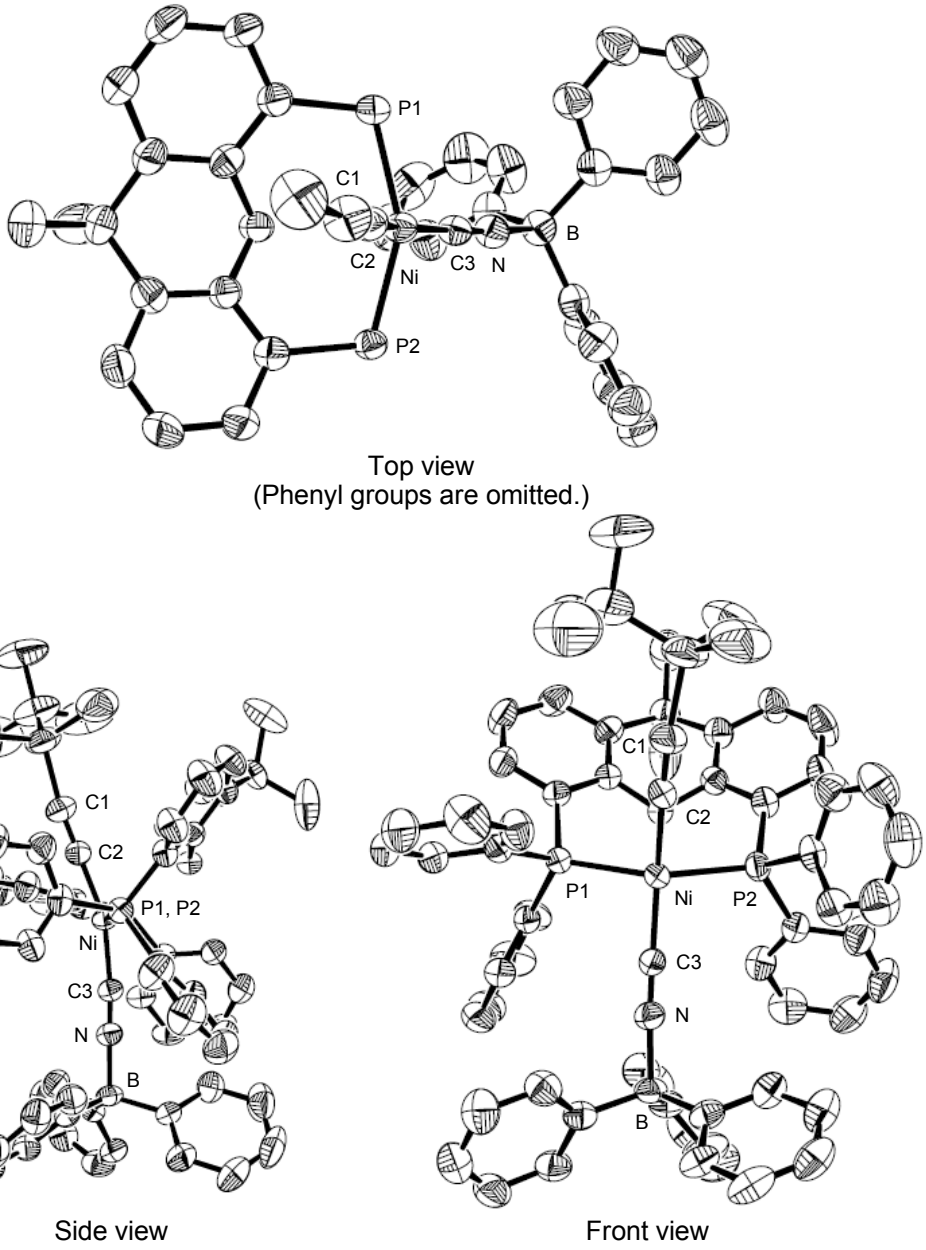
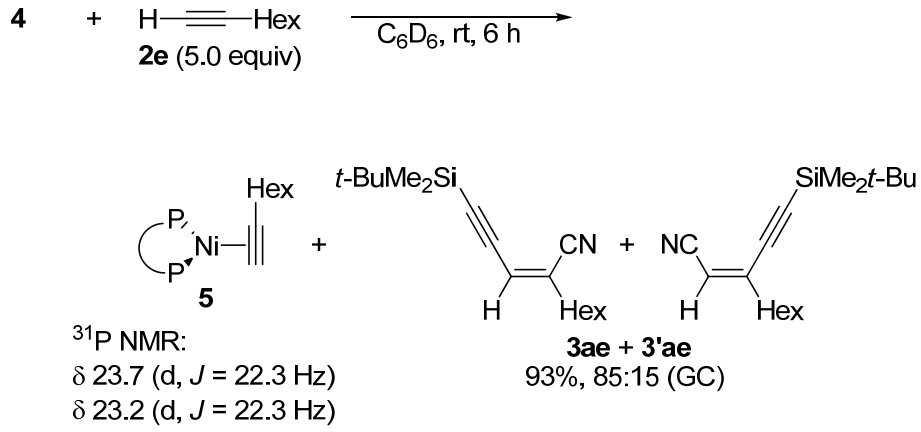


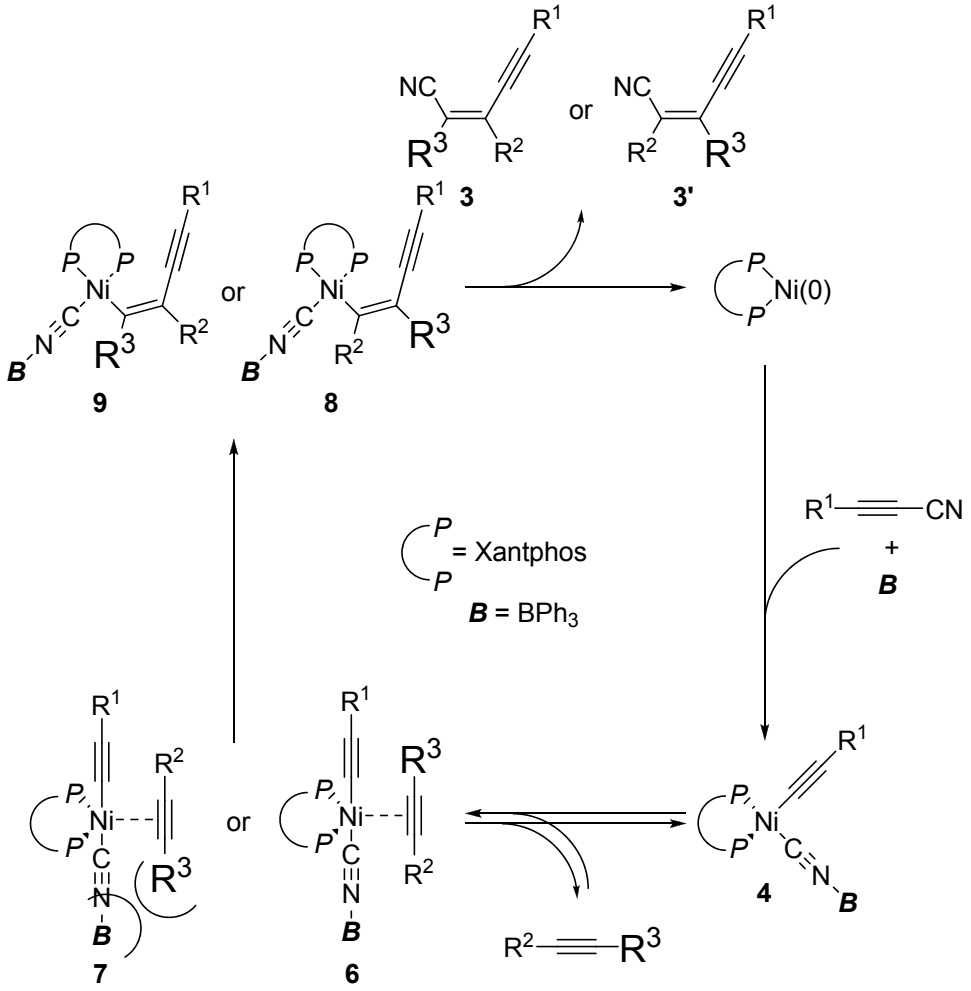
Figure 2. ORTEP drawings of **4**.

Thus, the catalytic cycle for the alkynylcyanation reaction should be initiated by oxidative addition of a C(sp)–CN bond to nickel(0) by the aid of BPh_3 to give **4** (Scheme 3). Coordination of an alkyne to the nickel center of **4** followed by migration of the alkynyl group in **6** or **7** to the alkyne gives *cis*-alkenylnickel intermediate **8** or **9**, which then reductively eliminates *cis*-alkynylcyanation product **3** or **3'**, respectively. With internal alkynes, the coordination of alkynes seems to be rate-determining to favor

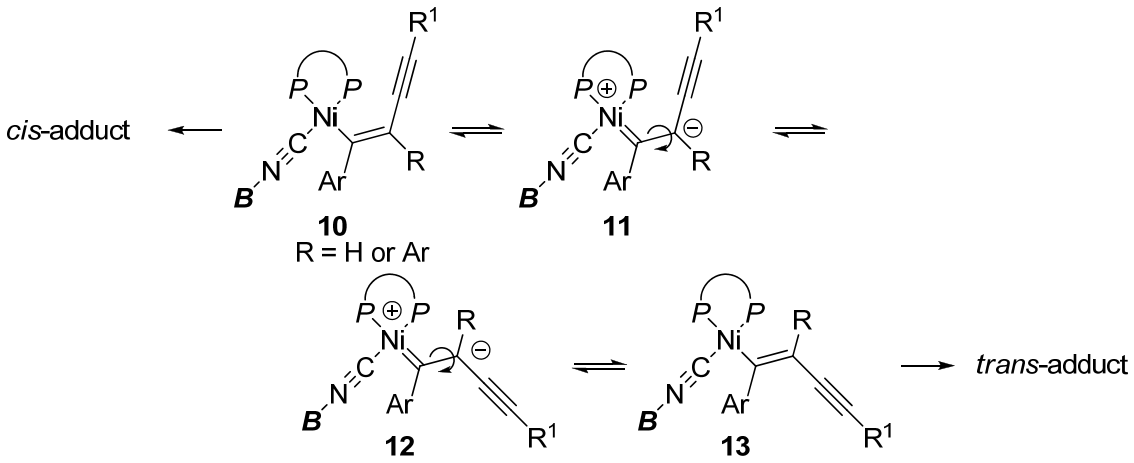
alkyne-coordinated nickel **6** to avoid steric repulsion between C≡N–***B*** and bulkier R^3 to give **3'** as a major product through **8**. Improved regioselectivity observed with **1h** over **1a** in the reaction with **2d** (entry 3 vs. entry 4, Table 3) may be rationally understood by this scenario. On the other hand, migration of the alkynyl group to the less-hindered alkyne carbon through **7** may be favored with terminal alkynes to give **9** and then finally **3** as a major product, because coordination of terminal alkynes to the nickel center is likely to be feasible. The excellent regioselectivity attained with **2i** (entry 9 of Table. 3) may indicate the presence of π-allylnickel-like stabilization in **9**. Such stabilization provided by an additional π-system connecting directly to an alkyne may also be important in the reactions of aryl-substituted alkynes, especially those having electron-donating aryl groups, to direct regioselective migratory insertion. Alternatively, an electron-withdrawing nature could also affect the regioselection by making the LUMO of the alkyne-terminus low enough to allow the nucleophilic alkynyl group to migrate selectively at this position. The trend of regioselectivities observed with arylacetylenes (entries 2–4 of Table 4) would be derived from the sum of those effects. Formation of *trans*-adducts could be ascribed to partial isomerization of *cis*-alkenylnickel intermediates **10** through nickel carbene species **11** or **12** (Scheme 4). Electron-donating aryl groups may facilitate this isomerization by stabilizing the transient nickel-carbene species having formal positive charge on nickel, thus favoring *trans*-adducts.



Scheme 2. Stoichiometric reaction of **4** with 1-octyne (**2e**).



Scheme 3. Plausible mechanism for the nickel/BPh_3-catalyzed alkynylcyanation of alkynes.



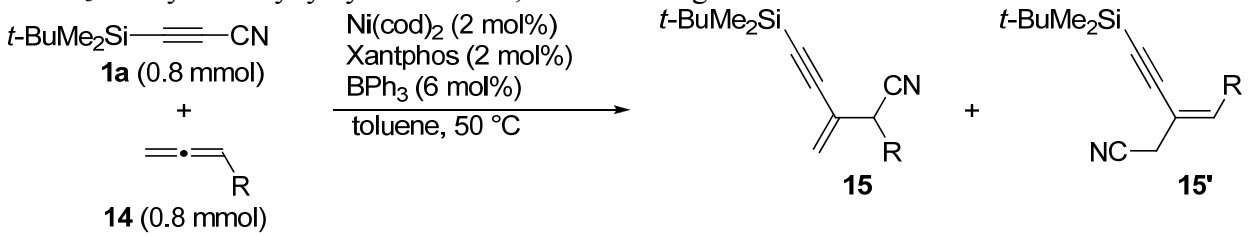
Scheme 4. Plausible mechanism for the formation of *trans*-alkynylcyanation products (**3aj**–**3al**).

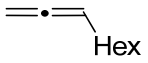
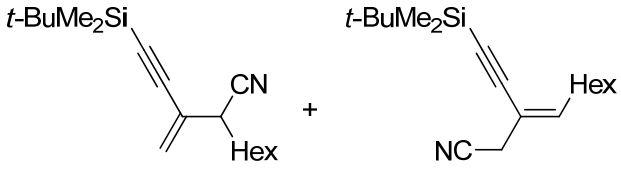
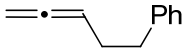
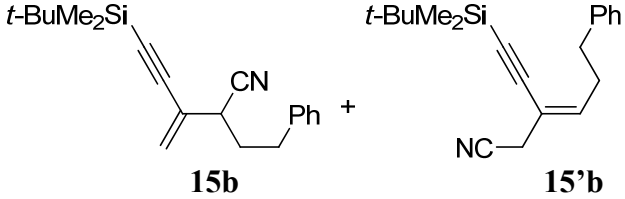
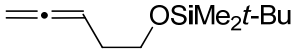
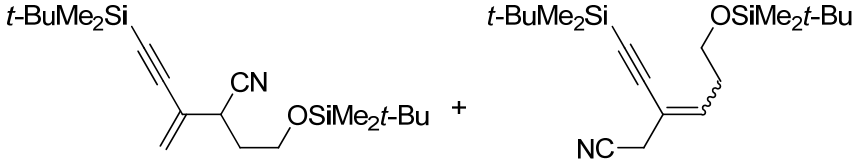
Nickel/BPh_3-catalyzed Alkynylcyanation of 1,2-Dienes

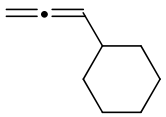
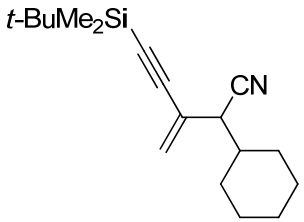
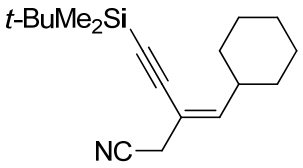
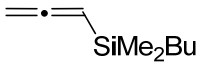
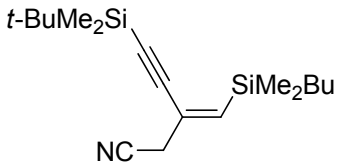
In the presence of the same catalyst, 1,2-dienes also underwent the alkynylcyanation. The reaction took place at an internal double bond of 1,2-dienes, and an alkynyl group was introduced to the cummulative carbon to give conjugated enynes **15** having a substituted cyanomethyl substituent (entries 1–4 of Table 5). On the other hand, silylallene **14e** showed opposite regioselectivity, giving (*Z*)-alkenylsilane **15'e** exclusively (entry 5). The reactions of propadiene and phenylallene gave no desired product due to rapid oligomerization of the allenes. The reactions of 1,1- and 1,3-di-substituted allenes such as 3-methyl-1,2-butadiene and 5,6-dodecadiene did not proceed and these 1,2-dienes were recovered intact due presumably to steric hindrance to prevent the dienes coordinating to the nickel center of **4** .

The catalytic cycle for the alkynylcyanation of 1,2-dienes shown in Scheme 5 should also be initiated by formation of **4**. The terminal double bond in 1,2-dienes coordinates to the nickel center to give **16**, and migratory insertion of the 1,2-diene takes place into the alkynyl–Ni bond to give a π-allylnickel species **18**, which may be thermodynamically more stable than **19**.[8] Reductive elimination of the allyl and cyano groups would give conjugated enynes **15**. Regioisomers **15'** may be formed through the coordination of **14** in an opposite direction to give **20**, followed by similar steps through π-allylnickel intermediates. However, **20** should be sterically unfavored. A bulky silyl group for R may inhibit C–C bond-forming reductive elimination from **18**. Instead, reductive elimination from **19** could be operative to afford **15'** with particular 1,2-diene **14e**.

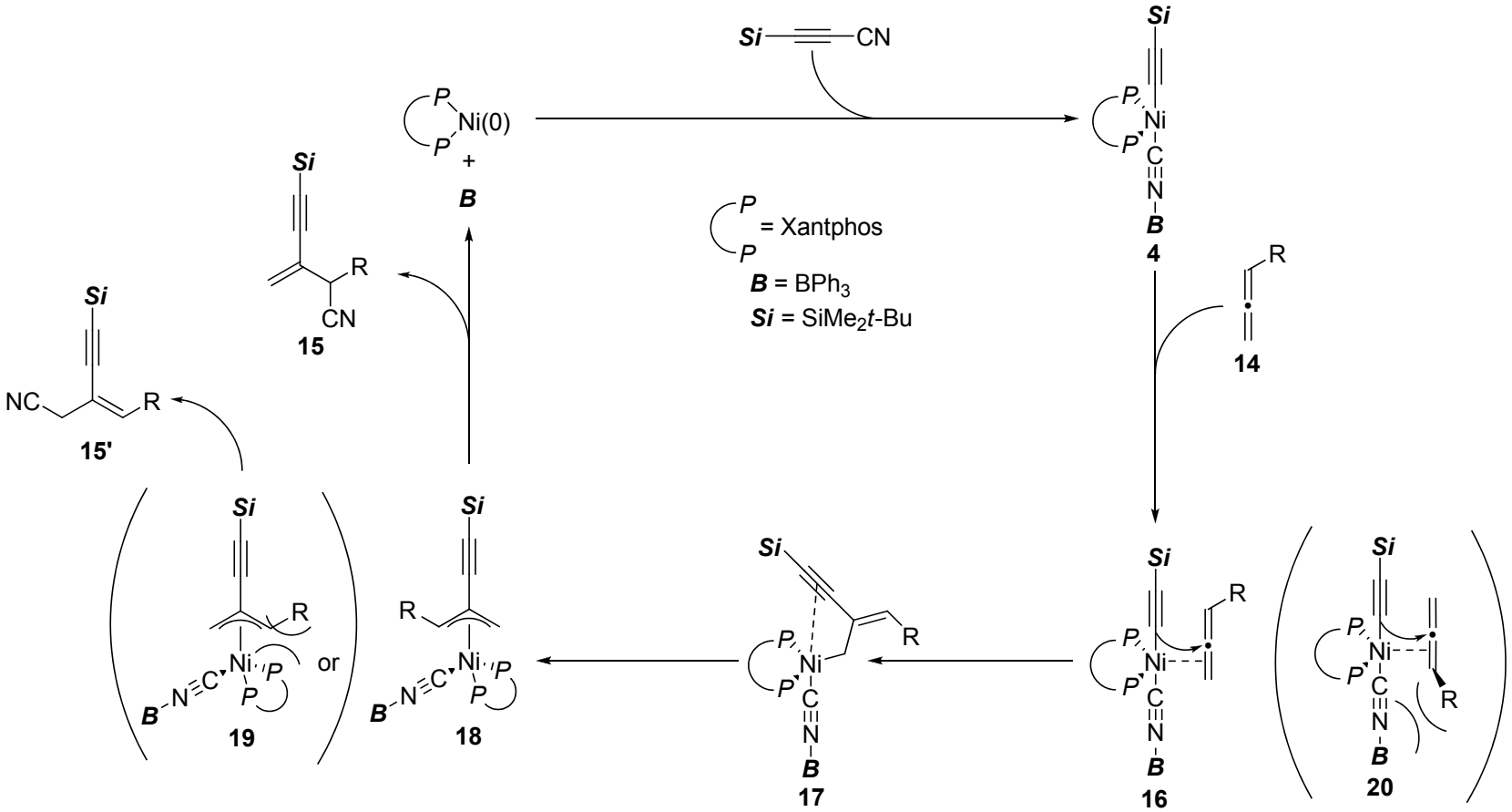
Table 5. Nickel/BPh_3-catalyzed alkynylcyanation of 1,2-dienes using **1a**[a]



Entry	**14**	Time (h)	Products	Yield[b] (**6**:**6'**)[c]
1	 **14a**	19	 **15a** + **15'a**	73 (93:7)[d]
2	 **14b**	24	 **15b** + **15'b**	82 (91:9)
3	 **14c**	17	 **15c** + **15'c**	75 (92:8)[e]

4	 **14d**	59	 **15d** +  **15'd**	74 (>95:5)[d]
5	 **14e**	66	 **15'e**	55 (5:>95)

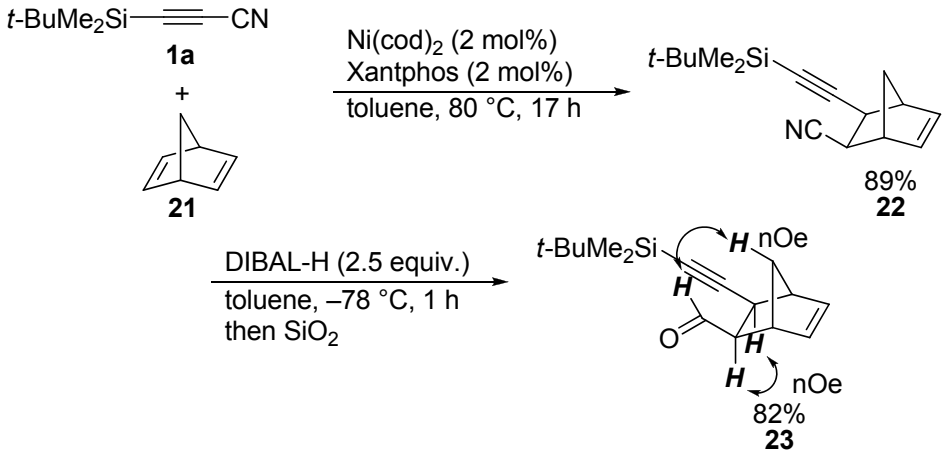
[a] All the reaction was carried out using **1a** (0.80 mmol), a 1,2-diene (0.80 mmol), $Ni(cod)_2$ (2.0 mol%), Xantphos (2.0 mol%), and BPh_3 (6.0 mol%) in toluene (0.80 mL). [b] Isolated yield. [c] Calculated based on yields of isolated products. [d] Estimated by ^1H NMR analysis of an isolated product. [e] *E*/*Z* = 11:89



Scheme 5. Plausible mechanism for the nickel/BPh_3-catalyzed alkynylcyanation of 1,2-dienes.

Nickel-catalyzed Alkynylcyanation of Norbornadiene

The author next turned his attention to the addition reaction of alkynyl cyanides across alkene substrate. Attempted reactions of alkynyl cyanide **1a** with simple alkenes including 1-octene, styrene, and 1,3-dodecadiene in the presence of a diverse range of nickel, a ligand, and a Lewis acid catalyst disappointedly gave no alkynylcyanation products in any detectable amounts. On the other hand, the reaction of **1a** with norbornadiene (**21**) took place in the presence of $Ni(cod)_2$ (2 mol%) and Xantphos (2 mol%) in toluene at 80 °C for 17 h to afford *exo*-*cis*-alkynylcyanation product **21** in 89% yield (Scheme 6).[9] The structure of **22** was assigned based on nOe experiments of ^{1}H NMR of aldehyde **23**, which was obtained by reduction of **22** (*vide infra*). Lewis acid cocatalysts were not effective for the alkynylcyanation of **20** to result in lower yields of **22**. Highly functionalized norbornene derivatives like **22** may find further applications as precursors for functionalized cyclopentanes[9c] or monomers for functionalized cyclic olefin polymers through ring-opening metathesis polymerization.[10]



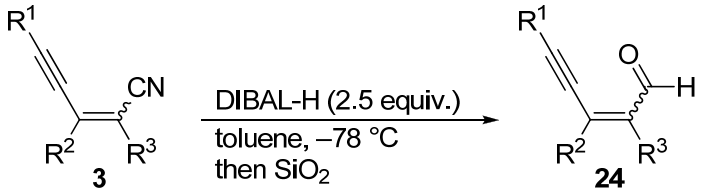
Scheme 6. Nickel-catalyzed alkynylcyanation of norbornadiene (**21**).

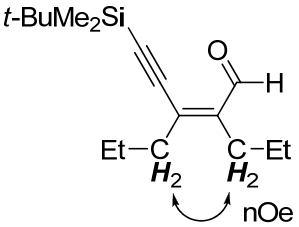
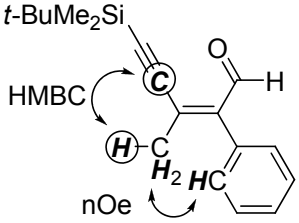
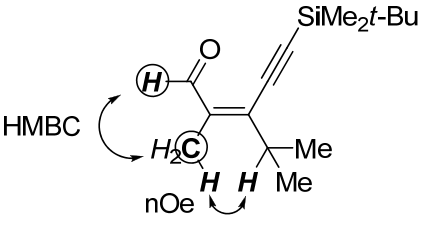
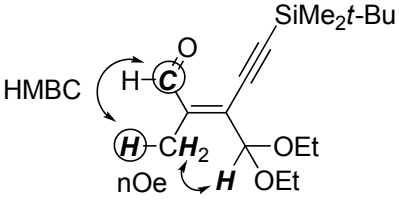
Transformations of alkynylcyanation products

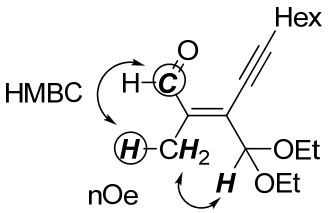
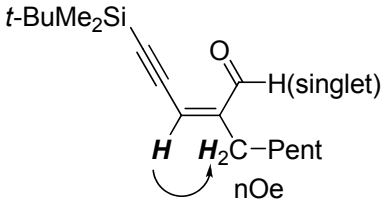
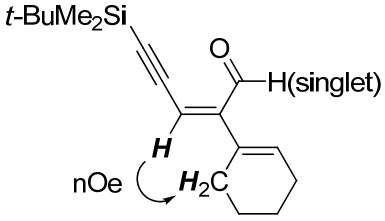
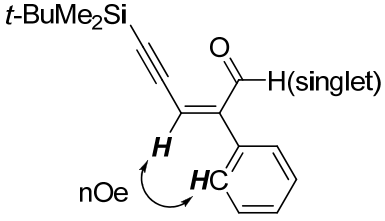
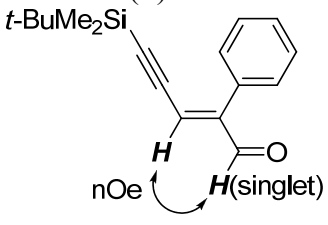
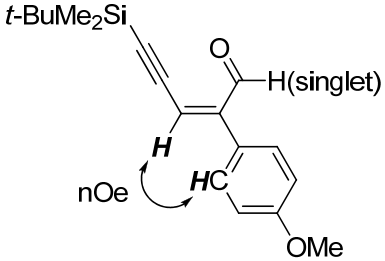
Reduction of the cyano group in alkynylcyanation products **3** to formyl was successfully performed with DIBAL-H with complete retention of stereochemistry (Table 6). This transformation was helpful to characterize the structures of **3** by nOe and ^{1}H–^{1}H couplings in ^{1}H NMR and/or HMBC experiments, because signals for two allylic methylenes appear separately in ^{1}H NMR. The resulting formyl group in **24da** was further transformed to afford highly substituted allylic alcohol **25** upon treatment

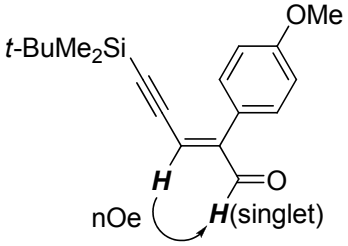
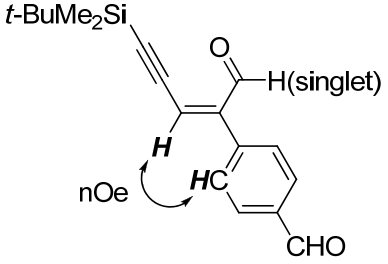
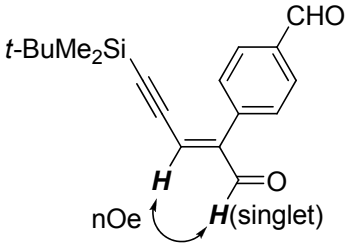
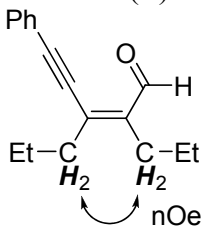
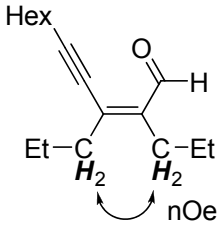
with a Grignard reagent (Scheme 7). Aldehydes **24** and allylic alcohols **25** have been demonstrated to serve as versatile synthetic intermediates for a variety of highly substituted cyclic compounds.[11]

Table 6. Reduction of **3** with DIBAL-H[a]

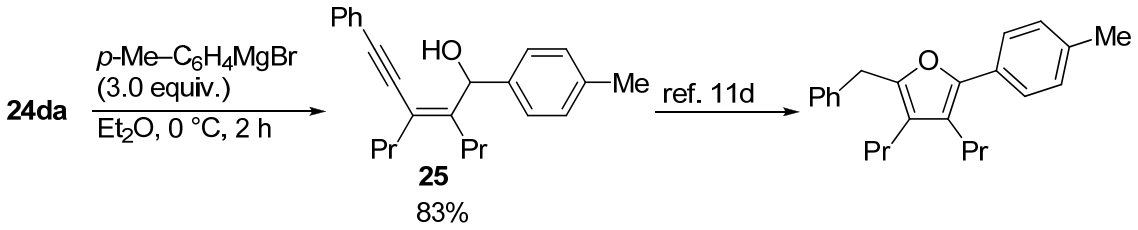


Entry	**3**	Product	Yield (%)[a]
1	**3aa**	 **24aa**	91
2	**3ab**	 **24ab**	92
3	**3'ac**	 **24'ac**	92
4	**3'ad**	 **24'ad**	82

5	**3'hd**	 **24'hd**	42
6	**3ae**	 **24ae**	77
7	**3ai**	 **24ai**	80
8	(*Z*)-**3ak**	 (*Z*)-**24ak**	100
9	(*E*)-**3ak**	 (*E*)-**24ak**	77
10	(*Z*)-**3al**	 (*Z*)-**24al**	78

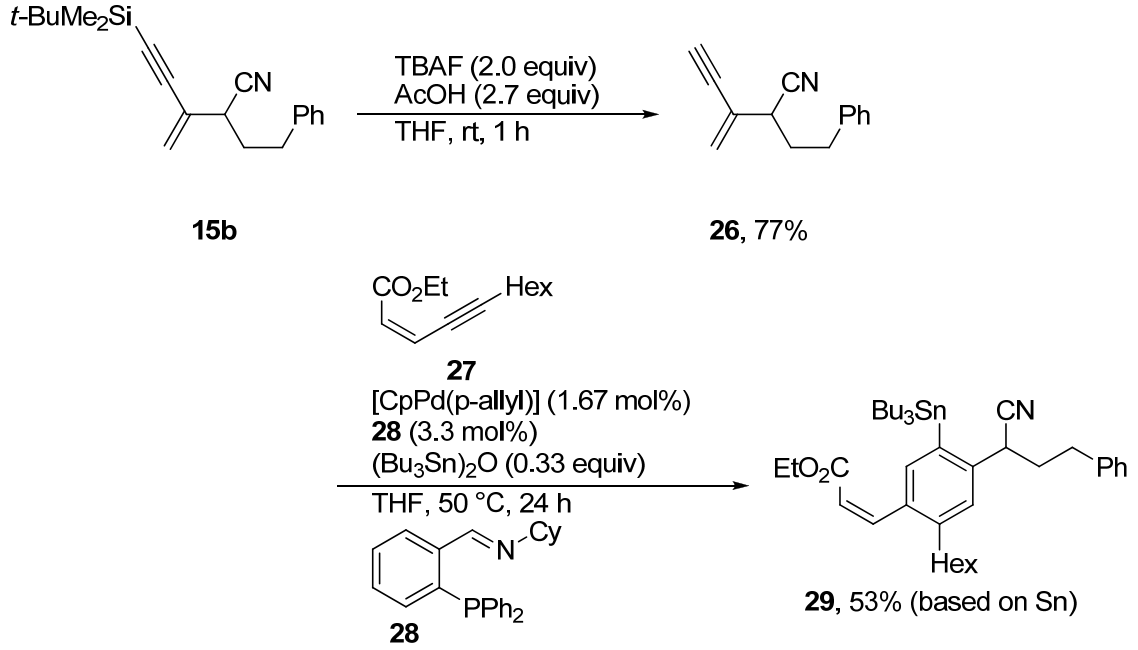
11	(*E*)-**3al**	 (*E*)-**24al**	94
12[b]	(*Z*)-**3am**	 (*Z*)-**24am**	80
13[b]	(*E*)-**3am**	 (*E*)-**24am**	69
14	**3da**	 **24da**	90
15	**3ha**	 **24ha**	80

[a] All the reaction was carried out using **3** and a 1.5 M solution of DIBAL-H in toluene (2.5 equiv) at –78 °C. Hydrolysis of the resulting imines was completed during silica gel column chromatography. [b] Isolated yield. [c] DIBAL-H (5.0 equiv) was used.



Scheme 7. Possible transformations of alkynylcyanation products

Desilylation of 1,2-diene-alkynylcyanation product **15b** followed by stannylative cross-cycloaddition reaction of the resulting **26** with ethyl (*Z*)-2-undecene-4-ynoate (**27**) in the presence of a palladium/iminophosphine **28** catalyst gave highly substituted phenylstannane **29** (Scheme 8).[12]



Scheme 8. Transformations of the 1,2-diene-alkynylcyanation product **15b**

In conclusion, the author has demonstrated alkynylcyanation reactions of alkynes and 1,2-dienes catalyzed by nickel/Xantphos/BPh_3. The transformations proceed with high stereo-, regio-, and chemoselectivities to afford a wide variety of highly functionalized conjugated enynes in an atom-economic manner. These enyne products are shown to serve as potent versatile synthetic precursors for various cyclic and linear compounds. He has also achieved stereoselective alkynylcyanation of norbornadiene to afford a highly functionalized norbornene. The catalytic cycles of the alkynylcyanation

reactions initiated by oxidative addition of alkynyl cyanides to nickel(0)/Xapntphos have been investigated in detail by isolation, structural characterization, and stoichiometric and catalytic reactions of *trans*-(xantphos)Ni($CNBPh_3$)(C≡C$SiMe_2$*t*-Bu) (**4**).

Experimental section

Chemicals. Anhydrous benzene was purchased from Nacalai Tesque degassed by bubbling an argon gas vigorously for 20 min before use. Benzene-d_6 was distilled from sodium/benzophenone ketyl. Alkynyl cyanides[4] and 1,2-dienes[13] were prepared according to the respective literature procedure.

Synthesis of alkynyl cyanides: ***A general procedure***

To a solution of a terminal alkyne (40 mmol) in diethyl ether (10 mL) was added a 1.6 M solution of *n*-BuLi (28 mL, 44 mmol) in hexane at –78 °C. The resulting reaction mixture was stired at –78 °C for 1 h, and then cyano phenolate (5.2 g, 44 mmol) was added. The reaction mixture was warmed up to room temperature and further stirred for 1 h before quenching with water. The aqueous layer was extracted with diethyl ether for three times. The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding alkynyl cyanides.

3-*tert*-Butyldimethylsilylpropynenitrile (1a). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (s, 9H), 0.21 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 104.9, 94.3, 76.6, 25.8, 16.6, –5.5; IR (neat) 2955, 2934, 2862, 2259, 2104, 1472, 1366, 1256, 1047, 966, 843, 824, 810, 783, 685, 581, 511, 459 cm^{-1}; HRMS (EI) Calcd for $C_9H_{15}NSi$: M^+, 165.0974. Found: *m/z* 165.0975.

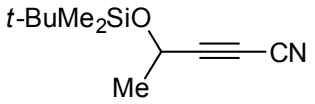
3-(Triethylsilyl)propynenitrile (1b). A colorless oil, R_f 0.28 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (q, J = 8.0 Hz, 9H), 0.71 (q, J = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 104.8, 93.8, 76.9, 7.3, 3.7; IR (neat) 2961, 2914, 2880, 2259, 2102, 1460, 1416, 1236, 1045, 1007, 964, 731 cm^{-1}; HRMS (EI) Calcd for $C_9H_{15}NSi$: M^+, 165.0974. Found: *m/z* 165.0979.

5-*tert*-Butyldimethylsilylpenta-2,4-diynenitrile (1c). An yellow oil, R_f 0.38 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.2, 93.0, 85.8, 67.4, 49.2, 25.9, 16.8, –5.3; IR (neat) 2955, 2932, 2860,

2239, 2179, 2079, 1472, 1254, 1209, 843, 824, 812, 781 cm^{-1}; HRMS (EI) Calcd for $C_{11}H_{15}NSi$: M^+, 189.0974. Found: *m/z* 189.0980.

2-Heptynedinitrile (1j). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 2.59 (t, *J* = 7.0 Hz, 2H), 2.52 (t, *J* = 7.0 Hz, 2H), 1.99 (quint, *J* = 7.0 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 117.9, 104.7, 84.0, 56.9, 23.2, 18.0, 16.4; IR (neat) 2957, 2874, 2315, 2263, 1762, 1686, 1599, 1454, 1425, 1350, 1329, 1312, 1296, 1215, 1074, 1042, 773 cm^{-1}; HRMS (FAB+) Calcd for $C_7H_6N_2$: M^+, 118.0531. Found: *m/z* 118.0535.

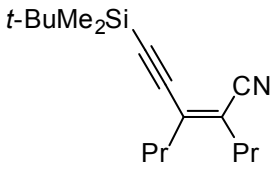
4-*tert*-Butyldimethylsiloxypent-2-ynenitrile (1k). A colorless oil, R_f 0.43 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.58 (q, *J* = 6.6 Hz, 1H), 1.48 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 104.7, 86.8, 58.9, 57.7, 25.7, 24.3, 18.2, –4.7, –4.9; IR (neat) 2957, 2932, 2888, 2861, 2311, 2280, 1748, 1472, 1464, 1445, 1391, 1371, 1362, 1339, 1308, 1260, 1153, 1109, 1028, 1005, 984, 939, 839, 829, 812, 781, 739, 667 cm^{-1}. Anal. Calcd for $C_{11}H_{19}NOSi$: C, 63.11; H, 9.15. Found: C, 63.32; H, 9.11.



Alkynylcyanation of alkynes: ***A general procedure***

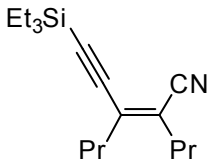
In a dry box, an alkynyl cyanide (1.00 mmol), an alkyne (1.00–2.0 mmol), and tetradecane (internal standard, 99 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (2.8–28 mg, 10.0–100 μmol), BPh_3 (7.3–73 mg, 30–300 μmol), and Xanthpos (5.8–58 mg, 10.0–100 μmol) in toluene (1.5 mL) placed in a vial, which was taken out from a dry box and heated at the temperature for the time specified in Tables 1–4. The resulting reaction mixture was filtered through a silica gel pad. The filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel to give the corresponding alkynylcyanation products in yields listed in Tables 1–4. Mixtures of regioisomers were further separated by preparative recycling silica gel chromatography to give isomerically pure products.

(*Z*)-3-*tert*-Butyldimethylsilylethynyl-2-propylhex-2-enenitrile (3aa). A brownish oil,



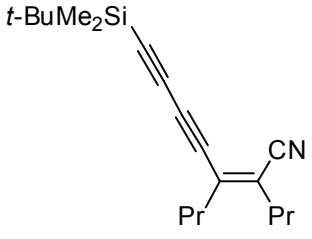
R_f 0.63 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (q, *J* = 7.2 Hz, 4H), 1.66–1.54 (m, 4H), 0.96 (s, 9H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 119.8, 118.7, 103.2, 102.0, 34.1, 31.9, 26.2, 21.7, 21.4, 16.8, 13.8, 13.7, –4.6; IR (neat) 2961, 2932, 2858, 2210, 2143, 1464, 1252, 1159, 839, 826, 812, 777, 735, 679 cm^{-1}; MS (EI) *m/z* (%) 261 (12), 260 (M^+–15, 52), 221 (11), 220 (66), 219 (83), 218 (100), 191 (11), 190 (23), 189 (15), 188 (13), 176 (11), 174 (12), 163 (10), 162 (16), 161 (22), 160 (65), 149 (16), 147 (14), 135 (19), 134 (16), 133 (55), 121 (13), 110 (16), 109 (13), 108 (11), 107 (16), 105 (12), 96 (10), 84 (30), 83 (22), 73 (32), 59 (41), 57 (29). Anal. Calcd for $C_{17}H_{29}NSi$: C, 74.11; H, 10.61. Found: C, 74.22; H, 10.60. The stereochemistry was assigned based on ^{1}H NMR nOe experiments of **24aa**.

(*Z*)-3-Triethylsilylethynyl-2-propylhex-2-enenitrile (3aa). A pale yellow oil, R_f 0.22



(hexane–ethyl acetate = 50 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (q, *J* = 7.1 Hz, 4H), 1.61 (sept, *J* = 7.3 Hz, 4H), 1.04 (t, *J* = 7.9 Hz, 9H), 0.96 (q, *J* = 7.0 Hz, 6H), 0.67 (q, *J* = 7.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 119.7, 118.7, 103.8, 101.2, 34.1, 31.9, 21.7, 21.4, 13.8, 13.7, 7.6, 4.4; IR (neat) 2961, 2876, 2212, 2143, 1458, 1416, 1381, 1236, 1157, 1005, 727 cm^{-1}. Anal. Calcd for $C_{17}H_{29}NSi$: C, 74.11; H, 10.61. Found: C, 74.13; H, 10.61.

(*Z*)-7-*tert*-Butyldimethylsilyl-2,3-dipropylhept-2-en-4,6-diynenitrile (3ca). An



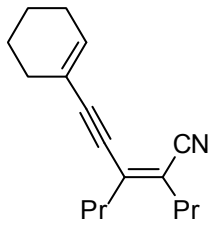
yellow oil, R_f 0.35 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (q, *J* = 8.1 Hz, 4H), 1.65–1.54 (m, 4H), 0.97 (s, 9H), 0.99–0.93 (m, 6H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 122.3, 118.4, 93.5, 87.6, 81.6, 73.8, 34.2, 32.2, 26.2, 21.6, 21.5, 16.9, 13.8, 13.6, –4.7; IR (neat) 2959, 2932, 2858, 2214, 2095, 1464, 1252, 1007, 920, 841, 827, 810, 777, 735, 681 cm^{-1}. Anal. Calcd for $C_{19}H_{29}NSi$: C, 76.19; H, 9.76. Found: C, 76.35; H, 9.85.

(*Z*)-3-Phenylethynyl-2propylhex-2-enenitrile (3da). A pale yellow oil, R_f 0.48 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.48 (m, 2H), 7.39–7.29 (m, 3H), 2.32 (q, *J* = 7.7 Hz, 4H), 1.74–1.58 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 132.0, 129.1, 128.4, 122.2, 119.1, 119.0, 97.2, 88.0, 34.0, 31.8, 21.6, 21.4, 13.7, 13.5; IR (neat) 2963, 2932, 2874, 2208, 1491, 756, 691 cm^{-1}. Anal. Calcd for $C_{17}H_{19}N$; C, 86.03; H, 8.07. Found: C, 85.73; H, 8.16. The stereochemistry was assigned based on ^{1}H NMR nOe experiments of **24da**.

(*Z*)-3-(4-Methoxyphenyl)ethynyl-2propylhex-2-enenitrile (3ea). A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 9.0 Hz, 2H), 6.85 (d, *J* = 9.0 Hz, 2H), 3.81 (s, 3H), 2.30 (q, *J* = 7.5 Hz, 4H), 1.74–1.56 (m, 4H), 0.98 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 139.4, 133.3, 119.1, 117.7, 114.0, 113.8, 97.4, 87.0, 55.2, 34.0, 31.7, 21.7, 21.5, 13.7, 13.5; IR (neat) 2963, 2872, 2185, 1607, 1508, 1458, 1290, 1252, 1173, 1032, 833 cm^{-1}. Anal. Calcd for $C_{18}H_{21}NO$; C, 80.86; H, 7.92. Found: C, 80.98; H, 68.01.

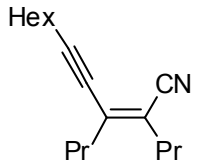
(*Z*)-3-(4-Chloroyphenyl)ethynyl-2propylhex-2-enenitrile (3fa). A pale yellow oil, R_f 0.23 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 3.36–2.28 (m, 4H), 1.72–1.57 (m, 4H), 1.00 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9, 135.1, 133.0, 128.6, 120.1, 119.4, 118.9, 95.8, 88.8, 34.0, 31.9, 21.8, 21.6, 13.8, 13.6; IR (neat) 2963, 2932, 2212, 1489, 1458, 1398, 1381, 1090, 1015, 829 cm^{-1}. Anal. Calcd for $C_{17}H_{18}NCl$; C, 75.13; H, 6.68. Found: C, 75.39; H, 6.83.

(*Z*)-5-(1-Cyclohexenyl)-2,3-dipropylpent-2-en-4-ynenitrile (3ga). A pale yellow oil,



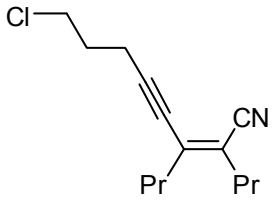
R_f 0.13 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.30–6.25 (m, 1H), 2.30–2.11 (m, 8H), 1.72–1.52 (m, 8H), 1.00–0.92 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.6, 137.4, 120.2, 119.2, 117.6, 99.3, 85.7, 34.2, 31.7, 28.9, 25.9, 22.2, 21.8, 21.51, 21.45, 13.8, 13.6; IR (neat): 2963, 2932, 2872, 2210, 2187, 1576, 1456, 1435, 1348, 918, 843, 799, 737 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{23}N$: M^+, 241.1830. Found: *m/z* 241.1833.

(*Z*)-2,3-Dipropylundec-2-en-4-ynenitrile (3ha). A brown oil, R_f 0.15 (hexane–ethyl



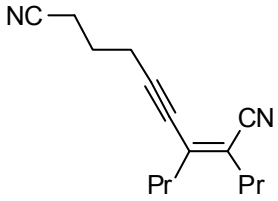
acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (t, *J* = 7.0 Hz, 2H), 2.27–2.18 (m, 4H), 1.65–1.24 (m, 12H), 0.95 (q, *J* = 7.7 Hz, 6H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 119.3, 117.4, 99.3, 79.4, 34.5, 31.7, 31.4, 28.6, 28.5, 22.6, 21.7, 21.5, 19.7, 14.2, 13.8, 13.6; IR (neat) 2961, 2932, 2872, 2206, 1589, 1458, 1379, 1329, 1111 cm^{-1}; Anal. Calcd for $C_{17}H_{27}N$; C, 83.20; H, 11.09. Found: C, 83.45; H, 11.00. The stereochemistry was assigned based on ^{1}H NMR nOe experiments of **24ha**.

(*Z*)-8-Chloro-2,3-dipropyloct-2-en-4-ynenitrile (3ia). A brown oil, R_f 0.22

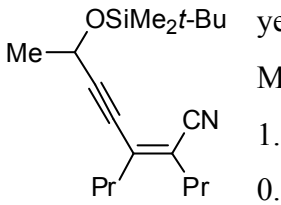


(hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (t, *J* = 6.2 Hz, 2H), 2.63 (t, *J* = 6.7 Hz, 2H), 2.28–2.18 (m, 4H), 2.05 (quint, *J* = 6.5 Hz, 2H), 1.65–1.53 (m, 4H), 0.96 (q, *J* = 5.0 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 119.1, 118.2, 96.6, 80.3, 43.5, 34.2, 31.5, 31.1, 21.6, 21.4, 17.0, 13.7, 13.5; IR (neat) 2963, 2874, 2206, 1589, 1458, 1290, 1231, 1113, 854, 656 cm^{-1}. Anal. Calcd for $C_{14}H_{20}ClN$: C, 70.72; H, 8.48. Found: C, 70.97; H, 8.41.

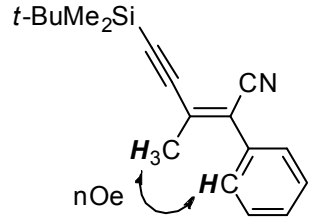
(*Z*)-8-Cyano-2,3-dipropyloct-2-en-4-ynenitrile (3ja). A pale yellow oil, R_f 0.30 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.62 (t, *J* = 6.6 Hz, 2H), 2.61 (t, *J* = 7.0 Hz, 2H), 2.25 (t, *J* = 7.6 Hz, 2H), 2.21 (t, *J* = 7.6 Hz, 2H), 1.95 (quint, *J* = 6.9 Hz, 2H), 1.65–1.51 (m, 4H), 0.96 (q, *J* = 7.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 119.2, 119.0, 118.9, 95.4, 81.2, 34.2, 31.6, 24.4, 21.7, 21.5, 18.7, 16.2, 13.8, 13.6; IR (neat) 2965, 2934, 2874, 2247, 2207, 1589, 1462, 1456, 1431, 1381, 1346, 1316, 1173, 1113, 1090, 889, 791, 741 cm^{-1}. Anal. Calcd for $C_{15}H_{20}N_2$: C, 78.90; H, 8.83. Found: C, 79.19; H, 8.95.



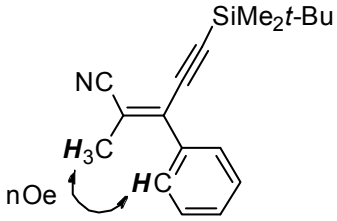
(*Z*)-6-*tert*-Butyldimethylsiloxy-2,3-dipropylhept-2-en-4-ynenitrile (3ka). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.73 (q, *J* = 6.5 Hz, 1H), 2.24 (q, *J* = 7.6 Hz, 4H), 1.67–1.53 (m, 4H), 1.49 (d, *J* = 6.6 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H), 0.92 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 118.8, 99.7, 81.6, 59.4, 34.2, 31.8, 25.9, 25.8, 25.3, 21.7, 21.4, 18.4, 13.8, 13.6, –4.5, –4.8; IR (neat) 2961, 2932, 2874, 2859, 2211, 1591, 1464, 1341, 1252, 1119, 1101, 1057, 988, 949, 835, 812, 779 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{24}NOSi$: $[M–(t\text{-Bu})]^+$, 262.1627. Found: *m/z* 262.1617.



(*Z*)-5-*tert*-Butyldimethylsilyl-3-methyl-2-phenylpent-2-en-4-ynenitrile (3ab). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.32 (m, 5H), 2.09 (s, 3H), 1.03 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 132.6, 128.9, 128.8, 128.6, 119.6, 118.3, 104.4, 104.2, 26.2, 20.9, 16.8, –4.7; IR (neat) 2955, 2930, 2885, 2858, 2214, 2127, 1580, 1493, 1472, 1445, 1373, 1364, 1252, 1227, 1005, 926, 839, 826, 812, 777, 766, 700, 677, 625, 588 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NSi$; C, 76.81; H, 8.24. Found (as a mixture with **3'ab**): C, 76.97; H, 8.40. The stereochemistry was assigned based on ^{1}H NMR nOe experiments, and the regiochemistry was determined based on HMBC experiments of **24ab**.

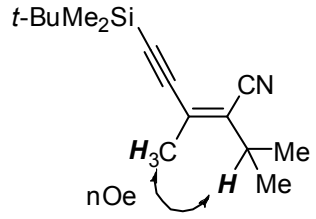


(*Z*)-5-*tert*-Butyldimethylsilyl-2-methyl-3-phenylpent-2-en-4-ynenitrile (3'ab). A



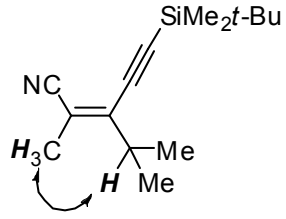
colorless solid, mp 65.2–65.6 °C, R_f 0.25 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.34 (m, 5H), 2.07 (s, 3H), 1.00 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5, 134.9, 129.1, 128.5, 128.3, 119.5, 115.0, 103.2, 103.0, 26.2, 18.3, 16.8, –4.7; IR (KBr) 2951, 2926, 2883, 2856, 2212, 2143, 1566, 1491, 1470, 1448, 1439, 1389, 1362, 1296, 1275, 1250, 1103, 1072, 1007, 826, 812, 773, 721, 702, 677, 538, 455 cm^{-1}. The stereochemistry was assigned based on ^{1}H NMR nOe experiments.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-isopropyl-3-methylpent-2-en-4-ynenitrile (3ac). A



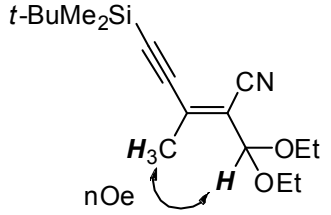
colorless oil, R_f 0.23 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (sept, J = 6.8 Hz, 1H), 1.99 (s, 3H), 1.14 (d, J = 6.8 Hz, 6H), 0.99 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.0, 126.7, 116.9, 104.4, 100.7, 28.7, 26.2, 21.1, 19.1, 16.8, –4.6; IR (neat) 2957, 2930, 2858, 2212, 2143, 1464, 1364, 1277, 1252, 1026, 926, 876, 839, 824, 810, 777, 689 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NSi$; C, 72.81; H, 10.18. Found (as a mixture with **3'ac**): C, 73.02; H, 10.30. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.

(*Z*)-5-*tert*-Butyldimethylsilyl-3-isopropyl-2-methylpent-2-en-4-ynenitrile (3'ac). A



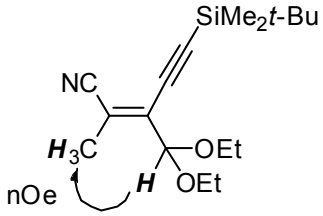
colorless oil, R_f 0.23 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77 (sept, J = 6.7 Hz, 1H), 1.97 (s, 3H), 1.10 (d, J = 6.8 Hz, 6H), 0.99 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.5, 119.4, 112.4, 103.6, 100.7, 29.8, 26.2, 20.9, 16.7, 16.1, –4.6; IR (neat) 2930, 2858, 2216, 2145, 1466, 1364, 1252, 1153, 1043, 1007, 914, 826, 777, 731, 675 cm^{-1}. The stereochemistry was assigned based on ^{1}H NMR nOe experiments, and the regiochemistry was determined by HMBC experiments of **24'ac**.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-diethoxymethyl-3-methylpent-2-en-4-ynenitrile



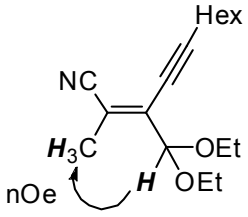
(3ad) A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.19 (s, 1H), 3.71–3.54 (m, 4H), 2.09 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 6H), 0.99 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3, 119.3, 116.3, 104.6, 103.5, 96.3, 61.7, 26.2, 19.9, 16.7, 15.1, –4.7; IR (neat) 2980, 2955, 2930, 2885, 2856, 2218, 2147, 1591, 1539, 1472, 1462, 1445, 1391, 1364, 1335, 1286, 1252, 1173, 1105, 1061, 1007, 934, 841, 826, 812, 777, 683, 665 cm^{-1}. Anal. Calcd for $C_{17}H_{29}NO_2Si$; C, 66.40; H, 9.51. Found (as a mixture with **3'ad**): C, 66.67; H, 9.35. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-methyl-3-diethoxymethylpent-2-en-4-ynenitrile



(3'ad). A pale yellow oil, R_f 0.10 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (s, 1H), 3.72–3.63 (m, 2H), 3.60–3.51 (m, 2H), 2.09 (s, 3H), 1.24 (t, *J* = 7.0 Hz, 6H), 0.98 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 118.8, 118.5, 105.1, 100.7, 98.0, 62.1, 26.1, 16.9, 16.8, 15.2, –4.7; IR (neat) 2976, 2955, 2930, 2885, 2858, 2218, 2145, 1578, 1541, 1472, 1462, 1445, 1391, 1373, 1364, 1337, 1286, 1252, 1167, 1113, 1063, 1007, 920, 841, 826, 812, 777 cm^{-1}. The stereochemistry was assigned based on ^{1}H NMR nOe experiments, and the regiochemistry was determined by HMBC experiments of **24'ad**.

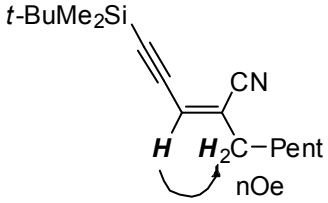
(*Z*)- 3-Diethoxymethyl-2-methylundec-2-en-4-ynenitrile (3'hd). A orange oil, R_f 0.33



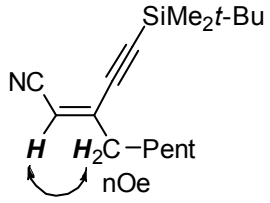
(hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.06 (s, 1H), 3.73–3.62 (m, 2H), 3.60–3.50 (m, 2H), 2.44 (t, *J* = 7.0 Hz, 2H), 2.07 (s, 3H), 1.60 (quint, *J* = 7.3 Hz, 2H), 1.52–1.16 (m, 6H), 1.24 (t, *J* = 7.0 Hz, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5, 119.2, 116.1, 102.2, 98.1, 77.1, 62.3, 31.4, 28.6, 28.3, 22.6, 20.2, 16.6, 15.2, 14.2; IR (neat) 2976, 2957, 2932, 2870, 2861, 2209, 1686, 1454, 1373, 1333, 1123, 1063, 764, 725, 696 cm^{-1}. Anal. Calcd for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81. Found: C, 73.73; H, 9.51. The stereochemistry was assigned based on ^{1}H NMR nOe

experiments, and the regiochemistry was determined by HMBC experiments of **24'hd**.

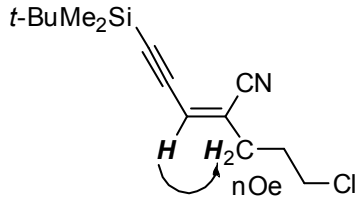
(*Z*)-5-*tert*-Butyldimethylsilyl-2-hexylpent-2-en-4-ynenitrile (3ae). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (s, 1H), 2.29 (t, *J* = 7.6 Hz, 2H), 1.62–1.50 (m, 2H), 1.39–1.23 (m, 6H), 0.99 (s, 9H), 0.90 (t, *J* = 6.6 Hz, 3H), 0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 126.0, 123.3, 117.1, 103.9, 100.1, 34.5, 31.5, 28.5, 27.9, 26.1, 22.6, 16.7, 14.1, –4.7; IR (neat) 2930, 2858, 2218, 1464, 1252, 1111, 1074, 841, 826, 812, 777 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{29}NSi$: M^+, 275.2069. Found: *m/z* 275.2061. The stereochemistry was assigned based on ^{1}H NMR nOe experiments, and the regiochemistry was determined by ^{1}H NMR spectra of **24ae**.



(*Z*)-5-*tert*-Butyldimethylsilyl-3-hexylpent-2-en-4-ynenitrile (3'ae). A colorless oil, R_f 0.13 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.43 (s, 1H), 2.28 (t, *J* = 7.5 Hz, 2H), 1.60–1.50 (m, 2H), 1.39–1.20 (m, 6H), 1.00 (s, 9H), 0.90 (t, *J* = 6.4 Hz, 3H), 0.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9, 116.5, 106.2, 103.2, 101.2, 37.4, 31.5, 28.5, 27.7, 26.1, 22.6, 16.7, 14.2, –4.7; IR (neat) 2930, 2858, 2220, 1585, 1466, 1364, 1252, 880, 839, 824, 808, 777 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{29}NSi$: M^+, 275.2069 Found: *m/z* 275.2069. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.



(*Z*)-5-*tert*-Butyldimethylsilyl-2-(3-chloroprop-1-yl)pent-2-en-4-ynenitrile (3af). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (t, *J* = 1.3 Hz, 1H), 3.56 (t, *J* = 6.1 Hz, 2H), 2.49 (td, *J* = 7.2, 1.0 Hz, 2H), 2.03 (quint, *J* = 6.7 Hz, 2H), 0.97 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 124.8, 123.6, 116.6, 105.0, 99.7, 43.2, 31.2, 30.2, 26.1, 16.6, –4.8; IR (neat) 2955, 2930, 2858, 2218, 1593, 1472, 1462, 1445, 1364, 1252, 1092, 1007, 841, 826, 777, 694, 681 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{22}ClNSi$: M^+, 267.1210.



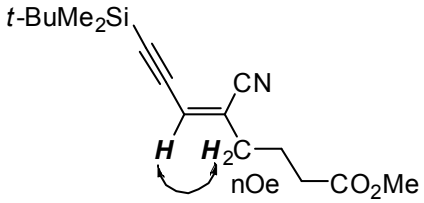
Found: *m/z* 267.1213. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.

(*Z*)-3-*tert*-Butyldimethylsilylethynyl-6-chloropent-2-enenitrile (3'af). A pale yellow oil, R_f 0.15 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.52 (t, *J* = 1.4 Hz, 1H), 3.56 (t, *J* = 6.2 Hz, 2H), 2.48 (td, *J* = 7.2, 1.2 Hz, 2H), 2.06 (quint, *J* = 7.0 Hz, 2H), 0.99 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 116.1, 107.1, 104.5, 100.5, 43.4, 34.2, 30.3, 26.1, 16.7, –4.8; IR (neat) 2955, 2930, 2858, 2220, 1587, 1472, 1445, 1364, 1252, 885, 866, 841, 824, 808, 779, 681 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{22}ClNSi$: M^+, 267.1210. Found: *m/z* 267.1209.

(*Z*)-8-*tert*-Butyldimethylsilyl-5-cyanopent-5-en-6-ynenitrile (3ag). A pale brown oil, R_f 0.15 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (s, 1H), 2.47 (t, *J* = 7.5 Hz, 2H), 2.41 (t, *J* = 7.0 Hz, 2H), 1.93 (quint, *J* = 7.2, 2H), 0.96 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 125.3, 122.7, 118.3, 116.2, 105.7, 99.5, 32.6, 26.0, 23.4, 16.6, 16.2, –4.9; IR (neat) 2955, 2930, 2858, 2247, 2218, 1595, 1462, 1364, 1252, 1094, 841, 826, 812, 777, 681 cm^{-1}. Anal. Calcd for $C_{15}H_{22}N_2Si$: C, 69.71; H, 8.58. Found: C, 69.84; H, 8.68. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.

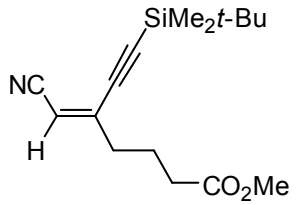
(*Z*)-3-*tert*-Butyldimethylsilylethynylhept-2-enedinitrile (3'ag). A pale brown oil, R_f 0.10 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 (t, *J* = 1.3 Hz, 1H), 2.47 (td, *J* = 5.3, 1.3 Hz, 2H), 2.41 (t, *J* = 7.0 Hz, 2H), 1.97 (quint, *J* = 7.2, 2H), 0.99 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.6, 118.4, 115.8, 107.9, 105.1, 100.0, 35.5, 26.1, 23.5, 16.7, 16.4, –4.8; IR (neat) 3055, 2953, 2930, 2858, 2247, 2220, 2147, 1589, 1464, 1364, 1252, 1157, 1007, 874, 841, 824, 808, 779, 681, 478 cm^{-1}; HRMS (FAB+) Calcd for $C_{15}H_{23}N_2Si$: $[M+H]^+$, 259.1631. Found: *m/z* 259.1635.

Methyl (*Z*)-8-*tert*-butyldimethylsilyl-5-cyano-oct-5-en-7-ynoate (3ah). A colorless oil,



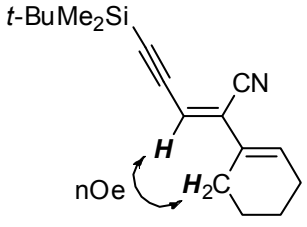
R_f 0.13 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (t, *J* = 1.4 Hz, 1H), 3.64 (s, 3H), 2.32 (t, *J* = 7.2 Hz, 4H), 1.87 (quint, *J* = 7.4, 2H), 0.94 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 124.5, 124.1, 116.6, 104.5, 99.8, 51.6, 33.3, 32.4, 26.0, 23.0, 16.5, –4.9; IR (neat) 2953, 2930, 2858, 2218, 1740, 1437, 1364, 1252, 1202, 1173, 1094, 1007, 841, 826, 812, 777, 683 cm^{-1}. Anal. Calcd for $C_{16}H_{25}NO_2Si$: C, 65.93; H, 8.65. Found (as a mixture with **3'ah**): C, 66.18; H, 8.66. The stereochemistry was assigned based on nOe experiments of ^{1}H NMR.

Methyl (*Z*)-7-*tert*-butyldimethylsilyl-5-cyanomethylenehept-6-ynoate (3'ah). A



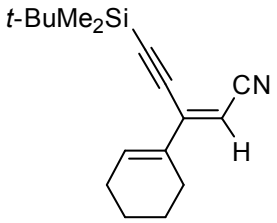
colorless oil, R_f 0.10 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (s, 1H), 3.69 (s, 3H), 2.40–2.31 (m, 4H), 1.92 (quint, *J* = 7.5 Hz, 2H), 0.99 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 145.4, 116.2, 106.9, 104.1, 100.7, 51.7, 36.3, 32.7, 26.1, 23.0, 16.7, –4.8; IR (neat) 2953, 2930, 2858, 2220, 1740, 1587, 1462, 1437, 1364, 1252, 1175, 1150, 1007, 872, 841, 824, 808, 779, 681 cm^{-1}.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-(cyclohexen-1-yl)pent-2-en-4-ynenitrile (3ai). A

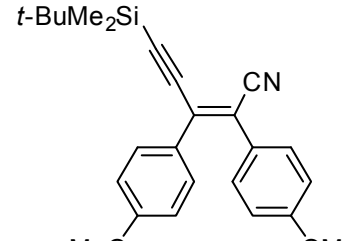


white solid, mp 71.3–72.7 °C, R_f 0.35 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (td, *J* = 4.4, 0.6 Hz, 1H), 6.03 (d, *J* = 0.7 Hz, 1H), 2.30–2.21 (m, 2H), 2.14–2.05 (m, 2H), 1.76–1.56 (m, 4H), 0.99 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.1, 131.4, 127.2, 116.3, 115.4, 106.2, 101.5, 26.1, 24.5, 22.1, 21.7, 16.7, –4.7; IR (KBr) 3032, 2930, 2856, 2226, 2129, 1620, 1470, 1462, 1448, 1433, 1362, 1254, 1096, 1080, 824, 681 cm^{-1}. Anal. Calcd for $C_{17}H_{25}NSi$: C, 75.21; H, 9.28. Found: C, 75.06; H, 9.20. The stereochemistry was assigned based on ^{1}H NMR nOe experiments. The regiochemistry was assigned based on ^{1}H NMR experiments of **24ai**.

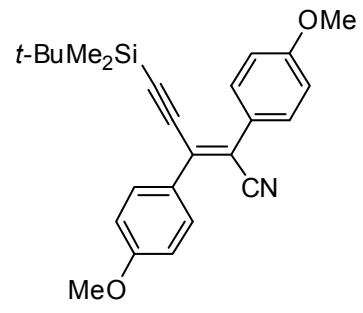
(*Z*)-5-*tert*-Butyldimethylsilyl-3-(cyclohexen-1-yl)pent-2-en-4-ynenitrile (3'ai). A pale yellow oil, R_f 0.38 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54–6.48 (m, 1H), 6.11 (s, 1H), 2.62–2.52 (m, 2H), 2.29–2.19 (m, 2H), 1.73–1.55 (m, 4H), 0.95 (s, 9H), 0.15 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.6, 132.3, 126.0, 118.6, 117.9, 109.7, 101.6, 27.3, 26.1, 26.0, 22.3, 21.4, 16.9, –4.8; IR (neat) 2930, 2858, 2224, 1616, 1556, 1470, 1462, 1433, 1250, 1194, 1092, 1072, 839, 824, 810, 777, 685, 633 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{25}NSi$: M^+, 271.1756. Found: *m/z* 271.1764.



(*Z*)-5-*tert*-Butyldimethylsilyl-2,3-di(4-methoxyphenyl)pent-2-en-4-ynenitrile [(*Z*)-3aj]. A yellow oil, R_f 0.33 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 3.80 (s, 6H), 1.03 (s, 9H), 0.23 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 159.7, 134.7, 131.0, 130.7, 127.4, 125.3, 119.3, 117.2, 114.0, 113.6, 104.5, 55.3, 31.7, 26.3, 16.9, –4.6; IR (neat) 2953, 2930, 2899, 2857, 2209, 2141, 1605, 1574, 1512, 1505, 1470, 1462, 1443, 1416, 1362, 1323, 1298, 1287, 1254, 1177, 1128, 1105, 1032, 1013, 984, 939, 878, 833, 812, 799, 777, 694, 683, 654, 633, 602, 571 cm^{-1}. Anal. Calcd for $C_{25}H_{29}NO_2Si$: C, 74.40; H, 7.24. Found: C, 74.22; H, 7.24.

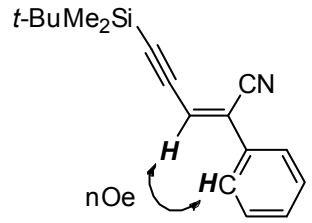


(*E*)-5-*tert*-Butyldimethylsilyl-2,3-di(4-methoxyphenyl)pent-2-en-4-ynenitrile ((*E*)-3aj). A white crystal, mp 96.2–96.4 °C, R_f 0.40 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.0 Hz, 2H), 7.73 (d, *J* = 9.0 Hz, 2H), 6.96 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.1 Hz, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 0.92 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 160.1, 134.3, 130.23, 130.17, 129.4, 126.5, 119.3, 116.4, 113.7, 113.5, 108.8, 103.9, 55.44, 55.40, 26.2, 16.9, –4.8; IR (KBr) 2951, 2930, 2857, 2205, 1605, 1578, 1541, 1512, 1466, 1441, 1418, 1360, 1323, 1306, 1277, 1256, 1179, 1113, 1078, 1047, 1022, 937, 837, 777, 768, 704,



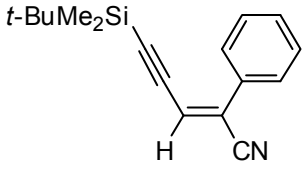
681, 586, 540, 527 cm^{-1}. Anal. Calcd for $C_{25}H_{29}NO_2Si$: C, 74.40; H, 7.24. Found: C, 74.56; H, 7.27. The stereochemistry was assigned based on X-ray crystallography. Colorless single crystals were obtained by recrystalization from methanol suitable for X-ray crystallographic analysis.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-phenylpent-2-en-4-ynenitrile [(*Z*)-3ak]. A white solid,

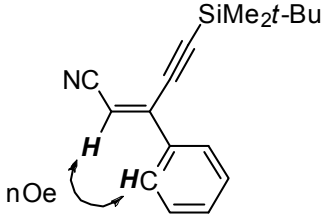


mp 75.1–75.9 °C, R_f 0.22 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.60–7.54 (m, 2H), 7.46–7.38 (m, 3H), 6.64 (s, 1H), 1.04 (s, 9H), 0.24 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.0, 130.1, 129.0, 125.5, 124.8, 120.8, 116.0, 108.3, 101.1, 26.2, 16.8, –4.7; IR (KBr) 3065, 3051, 3038, 3013, 2947, 2928, 2885, 2856, 2222, 2139, 1936, 1871, 1740, 1582, 1497, 1472, 1464, 1448, 1410, 1391, 1364, 1327, 1257, 1248, 1101, 1005, 978, 939, 908, 872, 829, 810, 772, 754, 679, 596, 502, 476, 434, 422 cm^{-1}. Anal. Calcd for $C_{17}H_{21}NSi$: C, 76.35; H, 7.91. Found [as a mixture with (*E*)-**3ak** and **3'ak**]: C, 76.45; H, 7.87. The stereochemistry was assigned based on ^1H NMR nOe experiments. The regiochemistry was determined by ^1H NMR experiments of (*Z*)-**24ak**.

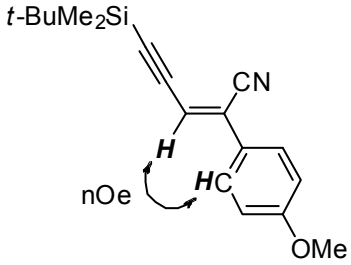
(*E*)-5-*tert*-Butyldimethylsilyl-2-phenylpent-2-en-4-ynenitrile [(*E*)-3ak]. A pale



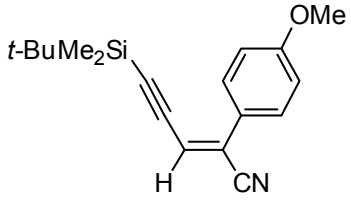
yellow oil, R_f 0.30 (hexane–ethyl acetate = 30 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.05–7.98 (m, 2H), 7.44–7.39 (m, 3H), 6.46 (s, 1H), 0.97 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.7, 130.2, 128.3, 127.9, 123.5, 121.1, 118.8, 111.5, 101.0, 26.1, 16.9, –4.8; IR (neat) 2953, 2928, 2897, 2856, 2218, 1583, 1560, 1541, 1497, 1470, 1445, 1412, 1364, 1252, 1202, 1086, 1070, 1007, 839, 824, 812, 770, 689, 667 cm^{-1}; The stereo- and regiochemistry was assigned based on ^1H NMR nOe experiments of (*E*)-**24ak**.

(*Z*)-5-*tert*-Butyldimethylsilyl-3-phenylpent-2-en-4-ynenitrile (3'ak). A white solid, 

mp 58.7–59.2 °C, R_f 0.15 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.64 (m, 2H), 7.49–7.41 (m, 3H), 6.00 (s, 1H), 1.05 (s, 9H), 0.27 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.6, 134.1, 130.8, 128.7, 126.6, 117.1, 107.8, 101.2, 100.1, 26.2, 16.8, –4.7; IR (KBr) 3055, 2949, 2926, 2883, 2855, 2214, 2152, 1618, 1582, 1556, 1493, 1470, 1450, 1408, 1389, 1360, 1344, 1333, 1313, 1252, 1184, 1067, 1026, 1005, 970, 947, 835, 804, 768, 692, 679, 664, 642, 592, 517, 444, 413 cm^{-1}; The stereochemistry was assigned based on ^{1}H NMR nOe experiments.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-(4-methoxyphenyl)pent-2-en-4-ynenitrile [(*Z*)-3al]. 

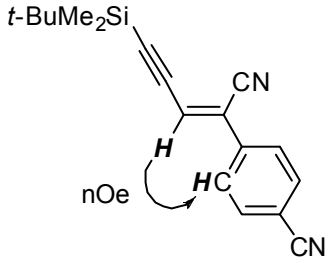
A yellow solid, mp 55.7–56.3 °C, R_f 0.12 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 9.0 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.51 (s, 1H), 3.84 (s, 3H), 1.02 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 127.0, 124.6, 124.4, 118.2, 116.2, 114.4, 107.0, 101.4, 55.5, 26.2, 16.8, –4.7; IR (KBr) 3059, 3032, 3007, 2926, 2855, 2224, 2133, 1879, 1744, 1609, 1576, 1512, 1464, 1443, 1421, 1410, 1391, 1362, 1333, 1319, 1285, 1254, 1186, 1119, 1101, 1034, 1011, 974, 937, 876, 824, 810, 773, 754, 681, 637, 625, 588, 519 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NOSi$: C, 72.68; H, 7.79. Found [as a mixture with (*E*)-**3al**]: C, 72.62; H, 7.79. The stereochemistry was determined by ^{1}H NMR nOe experiments, and the regiochemistry was assigned based on ^{1}H NMR experiments of (*Z*)-**24al**.

(*E*)-5-*tert*-Butyldimethylsilyl-2-(4-methoxyphenyl)pent-2-en-4-ynenitrile [(*E*)-3al]. 

A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.32 (s, 1H), 3.86 (s, 3H), 0.98 (s, 9H), 0.19 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 129.5, 124.5, 122.9, 119.0, 118.3, 113.7, 110.6, 101.5, 55.5, 26.2, 16.9, –4.8; IR (neat) 2953, 2930, 2897, 2856, 2218, 1605, 1580, 1555, 1514, 1464, 1443, 1420, 1364, 1304,

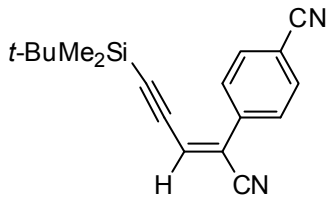
1259, 1205, 1182, 1078, 1049, 1028, 1007, 939, 835, 831, 810, 777, 685, 631, 519 cm^{-1}; The stereo- and regiochemistries were assigned based on ^1H NMR nOe experiments of (*E*)-**24al**.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-(4-cyanophenyl)pent-2-en-4-ynenitrile [(*Z*)-3am]. A



white solid, mp 113.7–114.2 °C, R_f 0.20 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 2H), 7.67 (d, *J* = 8.8 Hz, 2H), 6.76 (s, 1H), 1.01 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 132.7, 126.0, 124.0, 123.0, 117.8, 115.2, 113.6, 111.9, 100.5, 26.1, 16.8, –4.8; IR (KBr) 3098, 3065, 3026, 2953, 2926, 2885, 2856, 2230, 2135, 1935, 1605, 1572, 1558, 1506, 1470, 1462, 1441, 1416, 1391, 1362, 1333, 1319, 1252, 1186, 1097, 1005, 976, 937, 889, 841, 812, 779, 683, 602, 550, 479, 453, 426 cm^{-1}. Anal. Calcd for $C_{18}H_{20}N_2Si$: C, 73.92; H, 6.89. Found: C, 73.73; H, 6.89. The stereochemistry was assigned based on ^1H NMR nOe experiments, and the regiochemistry was assigned based on ^1H NMR experiments of (*Z*)-**24am**.

(*E*)-5-*tert*-Butyldimethylsilyl-2-(4-cyanophenyl)pent-2-en-4-ynenitrile [(*E*)-3am]. A

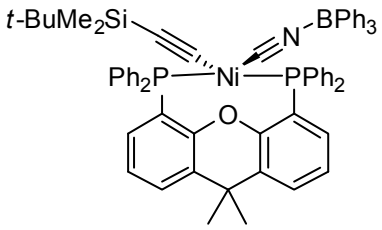


colorless oil, R_f 0.25 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 6.61 (s, 1H), 0.97 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 132.1, 128.4, 124.1, 121.6, 117.9, 117.8, 114.7, 113.6, 100.3, 26.1, 16.9, –4.9; IR (neat) 3021, 2953, 2930, 2886, 2859, 2232, 1609, 1578, 1547, 1508, 1470, 1464, 1408, 1364, 1252, 1207, 1078, 1007, 912, 843, 824, 812, 779, 735, 685, 631, 540 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{20}N_2Si$: M^+, 293.1474. Found: *m/z* 293.1463. The stereo- and regiochemistries were assigned based on ^1H NMR nOe experiments of (*E*)-**24am**.

Sythesis of *trans*-(xantphos)Ni(CNBPh$_3$)(C≡CSiMe$_2$*t*-Bu) (4)

To a benzene solution (3.5 mL) of $Ni(cod)_2$ (138 mg, 0.50 mmol) and Xanthpos (145 mg, 0.50 mmol) were added **1a** (83 mg, 0.50 mmol) and BPh_3 (121 mg, 0.50

mmol) in a dry box at room temperature. The resulting dark red solution was concentrated *in vacuo*, and the resulting precipitates were washed with hexane to give *trans*-(xantphos)Ni(CNBPh$_3$)(C≡CSiMe$_2$*t*-Bu) (**4**, 439 mg, 84%) as a brown powder, ^{1}H

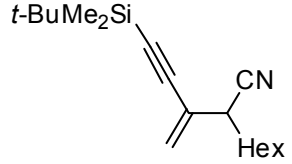


NMR (400 MHz, C_6D_6) δ 8.10–7.96 (br m, 4H), 7.55 (q, J = 6.2 Hz, 4H), 7.30–6.94 (m, 25H), 6.86 (t, J = 7.5 Hz, 2H), 6.76 (t, J = 7.6 Hz, 2H), 6.70 (t, J = 7.7 Hz, 4H), 1.49 (s, 3H), 1.26 (s, 3H), 0.36 (s, 9H), –0.46 (s, 6H); ^{13}C NMR (101 MHz, C_6D_6) δ 155.9 (t, $J_{C–P}$ = 5.9 Hz), 155.3 (br, s), 136.3 (t, $J_{C–P}$ = 6.1 Hz), 136.1, 135.1, 133.8 (t, $J_{C–P}$ = 23.0 Hz), 133.6 (t, $J_{C–P}$ = 5.8 Hz), 131.9, 131.5, 131.3, 129.9 (t, $J_{C–P}$ = 5.0 Hz), 129.2 (t, $J_{C–P}$ = 5.4 Hz), 128.5, 128.2, 127.4, 125.1, 125.0, 124.8 (t, $J_{C–P}$ = 26.8 Hz), 122.8 (t, $J_{C–P}$ = 44.1 Hz), 37.1, 33.9, 27.1, 24.5, 17.1, –3.1; ^{31}P NMR (121 MHz, C_6D_6) δ 15.7 (s); IR (KBr) 3414, 3061, 2953, 2924, 2851, 2180, 2035, 1586, 1481, 1435, 1404, 1242, 1213, 1096, 826, 745, 702, 617, 530, 519, 471 cm^{-1}. Dark red single crystals were obtained by recrystalization from hexane and dichloromethane suitable for X-ray crystallographic analysis.

Alkynylcyanation of 1,2-dienes: ***A general procedure***

In a dry box, a solution of **1a** (132 mg, 0.8 mmol) and a 1,2-diene (0.80 mmol) in toluene and a solution of BPh_3 (11.6 mg, 48 μmol) in toluene (0.40 mL) were added successively to a solution of Ni(cod)$_2$ (4.4 mg, 16 μmol) and Xanthpos (9.3 mg, 16 μmol) in toluene (0.40 mL) placed in a vial. The vial was taken outside the dry box and heated at 50 °C for the time both specified in Table 5. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give the corresponding alkynylcyanation products in yields listed in Table 5.

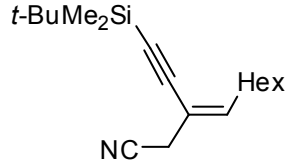
2-(4-*tert*-Butyldimethylsilyl-1-buten-3-yl)octanenitrile (15a). A pale yellow oil, R_f



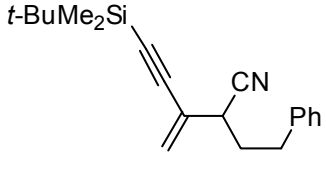
0.23 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 1H), 5.61 (s, 1H), 3.31 (t, J = 7.0 Hz, 1H), 1.94–1.78 (m, 2H), 1.56–1.22 (m, 8H), 0.96 (s, 9H), 0.90 (t, J =

6.9 Hz, 3H), 0.153 (s, 3H), 0.150 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 126.2, 124.2, 119.0, 102.0, 96.0, 38.3, 31.9, 31.5, 28.7, 26.5, 26.2, 22.6, 16.8, 14.2, –4.6; IR (neat) 2955, 2930, 2858., 2247, 2152, 1612, 1466, 1364, 1252, 1007, 914, 839, 826, 810, 777, 737, 681 cm^{-1}. Anal. Calcd for $C_{18}H_{31}NSi$; C, 74.67; H, 10.79. Found (as a mixture with **15'a**): C, 74.96; H, 10.76.

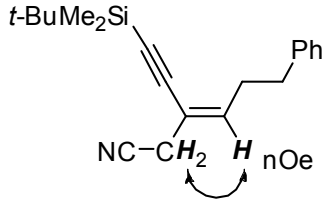
(*Z*)-3-(*tert*-Butyldimethylsilylethynyl)dec-3-enenitrile (15'a). A pale yellow oil, R_f 0.10 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 (tt, *J* = 7.5 Hz, 1.4 Hz, 1H), 3.20 (d, *J* = 1.1, 2H), 2.32 (q, *J* = 7.4 Hz, 2H), 1.48–1.24 (m, 8H), 0.97 (s, 9H), 0.90 (t, *J* = 6.8 Hz, 3H), 0.10 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 116.6, 112.2, 101.1, 99.1, 31.7, 30.8, 29.0, 28.6, 26.2, 25.0, 22.7, 16.7, 14.2, –4.5; IR (neat) 2955, 2930, 2856, 2147, 1464, 1252, 1007, 839, 810, 777, 683 cm^{-1}.



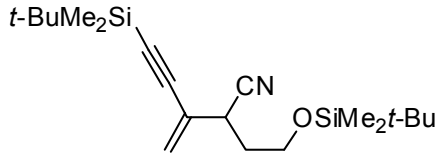
5-*tert*-Butyldimethylsilyl-3-methylene-2-(2-phenylethyl)pent-4-yne-nitrile (15b). A colorless oil, R_f 0.57 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.28 (m, 2H), 7.26–7.18 (m, 3H), 5.66 (d, *J* = 0.73 Hz, 1H), 5.64 (s, 1H), 3.32–3.25 (m, 1H), 2.90–2.72 (m, 2H), 2.30–2.10 (m, 2H), 0.96 (s, 9H), 0.160 (s, 3H), 0.155 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 128.5, 128.3, 126.3, 125.8, 124.6, 118.7, 101.8, 96.3, 37.5, 33.6, 32.6, 26.2, 16.7, –4.6; IR (neat) 3028, 2953, 2930, 2856, 2149, 1605, 1497, 1472, 1456, 1362, 1250, 914, 839, 826, 777, 748, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{27}NSi$; C, 77.61; H, 8.79. Found: C, 77.79; H, 8.56.



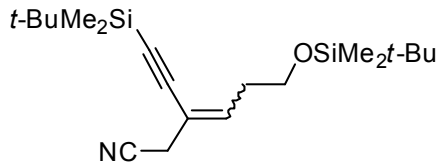
(*Z*)-3-(*tert*-Butyldimethylsilylethynyl)-6-phenylhex-3-enenitrile (15'b). A colorless oil, R_f 0.50 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 2H), 7.23–7.16 (m, 3H), 6.10 (tt, *J* = 7.3 , 1.5 Hz, 1H), 3.19 (d, *J* = 1.5 Hz, 2H), 2.78–2.71 (m, 2H), 2.70–2.61 (m, 2H), 0.97 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.84, 140.80, 128.3, 128.2, 125.9, 116.4, 113.1, 100.8, 99.7, 34.8, 32.5, 26.2, 25.0, 16.7, –4.5; IR (neat) 2953, 2930, 2856, 2253, 2149, 1497,



1458, 1364, 1252, 1007, 839, 777, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{27}NSi$; C, 77.61; H, 8.79. Found: C, 77.83; H, 8.86. The stereochemistry was assigned based on ^1H NMR nOe experiments.

5-*tert*-Butyldimethylsilyl-2-(2-*tert*-butyldimethylsiloxyethy-1-yl)-3-methylenepent-4-ynenitrile (15c). 

A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, *J* = 0.82 Hz, 1H), 5.61 (s, 1H), 3.82–3.71 (m, 2H), 3.59 (dd, *J* = 9.0, 5.9 Hz, 1H), 2.18–2.08 (m, 1H), 2.00–1.90 (m, 1H), 0.96 (s, 9H), 0.91 (s, 9H), 0.151 (s, 3H), 0.148 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 126.0, 124.5, 118.9, 101.8, 96.1, 59.2, 35.1, 34.9, 26.2, 25.9, 18.3, 16.7, –4.6, –5.26, –5.30; IR (neat) 2955, 2930, 2858, 2154, 1610, 1472, 1389, 1362, 1254, 1109, 1007, 939, 914, 837, 812, 777, 681 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{34}ONSi_2$: $[M–Me]^+$, 348.2179. Found: *m/z* 348.2191.

3-(*tert*-Butyldimethylsilylethynyl)-6-(*tert*-butyldimethylsiloxy)hex-3-enenitrile (15'c, *E*/*Z* = 11 : 89). 

A pale yellow oil, R_f 0.08 (hexane–ethyl acetate = 20:1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.13 (tt, *J* = 7.3, 1.5 Hz, 0.89H), 5.75 (tt, *J* = 4.8, 2.4 Hz, 0.11H), 3.69 (t, *J* = 6.6 Hz, 1.78H), 3.68 (t, *J* = 6.6 Hz, 0.22H), 3.21 (d, *J* = 1.5 Hz, 1.78H), 3.05 (d, *J* = 2.2 Hz, 0.22H), 2.55 (dt, *J* = 7.3, 6.6 Hz, 1.78H), 2.37 (dt, *J* = 7.3, 6.2 Hz, 0.22H), 1.04 (s, 0.99H), 0.99 (s, 0.99H), 0.97 (s, 8.01H), 0.90 (s, 8.01H), 0.39 (s, 0.66H), 0.36 (s, 0.66H), 0.15 (s, 5.34H), 0.07 (s, 5.34H); ^{13}C NMR (for *Z*-isomer, 101 MHz, $CDCl_3$) δ 138.7, 116.4, 113.7, 100.9, 99.6, 61.7, 34.5, 26.2, 26.0, 25.2, 18.4, 16.7, –4.5, –5.1; IR (neat) 2955, 2930, 2858, 2149, 1472, 1416, 1389, 1362, 1256, 1103, 939, 837, 810, 777, 685 cm^{-1}. Anal. Calcd for $C_{20}H_{37}NSi$; C, 66.05; H, 10.25. Found: C, 66.15; H, 10.26.

5-*tert*-Butyldimethylsilyl-2-cyclohexyl-3-methylpent-4-ynenitrile (15d). An yellow oil, R_f 0.25 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.64 (t, *J* = 0.6 Hz, 1H), 5.63 (dd, *J* = 1.2, 0.6 Hz, 1H), 3.18 (d, *J* = 5.0 Hz, 1H), 2.00–1.62 (m, 6H), 1.36–1.04 (m, 5H), 0.96 (s, 9H), 0.153 (s, 3H), 0.149 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 125.2, 125.0, 118.1, 102.3, 95.9, 45.1, 38.9, 31.4, 28.9, 26.19, 26.15, 25.9, 16.8, –4.6; IR (neat) 2930, 2856, 2249, 2149, 1470, 1450, 1362, 1252, 1007, 939, 839, 777, 683 cm^{-1}; HRMS (FAB+) Calcd for $C_{18}H_{30}NSi$: $[M+H]^+$, 288.2148. Found: *m/z* 288.2158.

(*Z*)-5-tert-Butyldimethylsilyl-3-butyldimethylsilylmethylenepent-4-ynentirile (15'e). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (t, *J* = 1.6 Hz, 1H), 3.30 (d, *J* = 1.6 Hz, 2H), 1.40–1.24 (m, 4H), 0.96 (s, 9H), 0.90 (t, *J* = 7.0 Hz, 3H), 0.75–0.40 (m, 2H), 0.19 (s, 6H), 0.15 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 126.2, 116.3, 103.8, 98.5, 29.0, 26.6, 26.2, 26.1, 16.8, 15.0, 14.0, –2.9, –4.7; IR (neat) 2955, 2930, 2858, 2143, 1578, 1472, 1464, 1414, 1250, 1111, 839, 826, 810, 777, 677 cm^{-1}. Anal. Calcd for $C_{18}H_{33}NSi_2$; C, 67.64; H, 10.41. Found: C, 67.44; H, 10.63. The regiochemistry was assigned based on ^{1}H NMR nOe experiments.

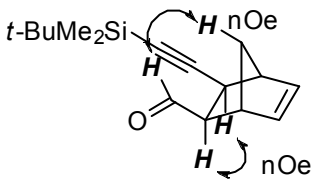
Alkynylcyanaiton of norbornadiene (21)

Alkynyl cyanide **1a** (165 mg, 1.00 mmol), **21** (92 mg, 1.00 mmol), and $C_{14}H_{29}$ (internal standard, 99 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (5.5 mg, 0.20 mmol) and Xanthpos (11.6 mg, 0.20 mmol) in toluene (1.00 mL) in a dry box. The vial was taken outside the dry box and heated at 80 °C for 17 h. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give (5*R**,6*S**) -6-(*tert*-butyldimethylsilylethynyl)-5-cyanobicyclo[2.2.1]hept-2-ene (**22**, 0.23 g, 89%) as an white solid, R_f 0.20 (hexane–ethyl acetate = 20 : 1), mp 58.9–59.3 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 5.6,

3.0 Hz, 1H), 6.11 (dd, *J* = 5.7, 3.1 Hz, 1H), 3.28 (s, 1H), 3.10 (s, 1H), 2.60 (dd, *J* = 8.6, 2.1 Hz, 1H), 2.56 (dd, *J* = 8.5, 1.8 Hz, 1H), 1.95 (d, *J* = 9.5 Hz, 1H), 1.65 (dt, *J* = 9.5, 1.9 Hz, 1H), 0.97 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 135.6, 120.2, 105.5, 87.7, 50.0, 48.1, 46.0, 35.5, 35.2, 26.2, 16.7, –4.4; IR (KBr) 2994, 2953, 2928, 2884, 2857, 2234, 2174, 1472, 1460, 1410, 1387, 1360, 1331, 1317, 1250, 1072, 1007, 939, 922, 912, 901, 837, 827, 775, 745, 714, 679, 631, 583, 529, 476 cm^{-1}. Anal. Calcd for $C_{16}H_{23}NSi$: C, 74.65; H, 9.00. Found: C, 74.74; H, 8.93. The stereochemistry was assigned based on ^{1}H NMR nOe experiments of **23**.

Reduction of 22 with DIBAL-H

To a solution of **22** (26 mg, 0.100 mmol) in toluene (1.00 mL) was added a 1.5 M solution of DIBAL–H in toluene (170 μL, 0.25 mmol) at –78 °C, and the resulting mixture was stirred at the same temperature for 1 h. The reaction was quenched with MeOH at –78 °C, and the resulting mixture was warmed at room temperature. The mixture was diluted with CH_2Cl_2 and filtered through a glass filter. The filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate as an eluent) to give (5*R**,6*S**)-6-(*tert*-butyldimethylsilylethynyl)-5-formylbicyclo[2.2.1]hept-2-ene (**23**, 21 mg, 82%) as a colorless oil, R_f 0.28 (hexane–ethyl acetate = 20 : 1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (d, *J* = 2.9 Hz, 1H), 6.17 (m, 2H), 3.17 (s, 1H), 3.06 (s, 1H), 2.67 (dd, *J* = 9.1, 1.8 Hz, 1H), 2.27 (dt, *J* = 9.3, 2.3 Hz, 1H), 1.81 (d, *J* = 9.1 Hz, 1H), 1.54 (dt, *J* = 9.1, 1.8 Hz, 1H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.7, 137.1, 136.9, 106.5, 87.0, 52.6, 50.2, 45.3, 43.7, 33.5, 26.1, 16.6, –4.4; IR (neat) 2953, 2928, 2884, 2857, 2729, 2172, 1724, 1472, 1462, 1391, 1362, 1329, 1250, 1076, 1007, 907, 839, 826, 812, 775, 733, 710, 681, 617 cm^{-1}; HRMS (EI) Calcd for $C_{12}H_{15}OSi$: $[M–(t\text{-Bu})]^+$, 203.0892. Found: *m/z* 203.0885.

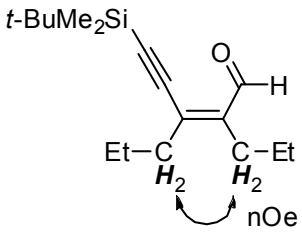


Reduction of 3 with DIBAL-H: ***A general procedure***

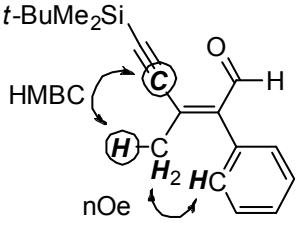
To a solution of **3** (0.20 mmol) in toluene (2.0 mL) was added a 1.5 M solution of DIBAL–H in toluene (0.33 mL, 0.5 mmol) at –78 °C, and the resulting mixture was

stirred at the same temperature for 1 h before quenching with MeOH at –78 °C. The mixture was warmed at room temperature, diluted with CH_2Cl_2 and filtered through a glass filter. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash chromatography on silica gel (hexane–ethyl acetate as an eluent) to give the corresponding aldehydes **24** in yields listed in Table 6.

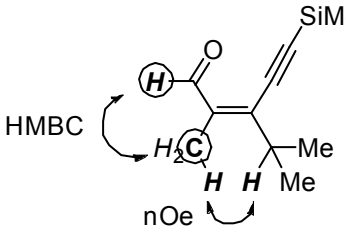
(*Z*)-3-(*tert*-Butyldimethylsilylethynyl)-2-propylhex-2-enal (24aa). An yellow oil, R_f 0.58 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 2.37 (t, *J* = 7.6 Hz, 2H), 2.26 (t, *J* = 7.9 Hz, 2H), 1.67 (sext, *J* = 7.4 Hz, 2H), 1.33 (sext, *J* = 7.6 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.95 (s, 9H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.15 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 146.4, 142.7, 104.5, 101.9, 35.8, 26.9, 26.1, 22.3, 21.3, 16.7, 14.2, 13.8, –4.8; IR (neat) 2961, 2932, 2858, 2139, 1678, 1585, 1464, 1250, 1167, 870, 839, 826, 777, 683 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{30}OSi$: M^+, 278.2066. Found: *m/z* 278.2059.



(*Z*)-5-*tert*-Butyldimethylsilyl-3-methyl-2-phenylpent-2-en-4-ynal (24ab). An pale yellow oil, R_f 0.68 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.5 (s, 1H), 7.43–7.31 (m, 3H), 7.11–7.06 (m, 2H), 2.08 (s, 3H), 1.01 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.0, 146.5, 139.3, 132.8, 129.4, 128.1, 128.0, 106.0, 102.6, 26.2, 23.0, 16.8, –4.6; IR (neat) 2953, 2930, 2856, 2727, 2124, 1686, 1583, 1470, 1443, 1383, 1371, 1304, 1252, 1219, 1070, 1018, 1007, 928, 908, 839, 826, 812, 777, 725, 700, 685, 648 cm^{-1}; HRMS (FAB+) Calcd for $C_{18}H_{24}OSi$: $[M+H]^+$, 285.1675. Found: *m/z* 285.1675.

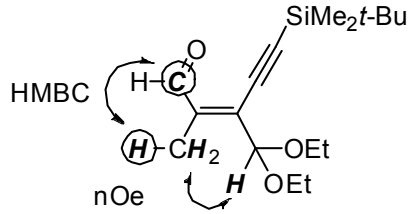


(*Z*)-5-*tert*-Butyldimethylsilyl-3-isopropyl-2-methylpent-2-en-4-ynal (24'ac). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 2.96 (sept, *J* = 6.7 Hz, 1H), 1.83 (s, 3H), 1.15 (d, *J* = 6.6 Hz, 6H), 0.97 (s, 9H), 0.16 (s, 6H); ^{13}C NMR (101



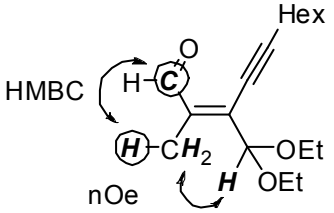
MHz, $CDCl_3$) δ 194.0, 148.5, 140.1, 105.6, 99.4, 31.2, 26.2, 20.7, 16.8, 10.3, –4.6; IR (neat) 2955, 2930, 2859, 2139, 1682, 1674, 1587, 1468, 1464, 1385, 1362, 1292, 1250, 1192, 1161, 1036, 1007, 922, 839, 826, 812, 777, 735, 689, 665, 592 cm^{-1}; Anal. HRMS (EI) Calcd for $C_{11}H_{17}OSi$: $[M–(t\text{-Bu})]^+$, 193.1049. Found: *m/z* 193.1057.

(*Z*)-5-*tert*-Butyldimethylsilyl-3-diethoxymethyl-2-methylpent-2-en-4-ynal (24'ad). A



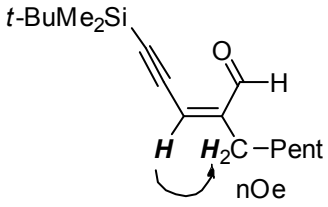
pale yellow oil, R_f 0.18 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 5.22 (s, 1H), 3.76–3.67 (m, 2H), 3.65–3.55 (m, 2H), 1.92 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 6H), 0.97 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.6, 144.1, 138.6, 107.1, 98.9, 98.8, 62.1, 26.2, 16.9, 15.3, 10.8, –4.7; IR (neat) 2976, 2953, 2930, 2885, 2856, 2143, 1682, 1593, 1472, 1462, 1445, 1383, 1364, 1339, 1296, 1250, 1169, 1134, 1115, 1061, 1007, 922, 839, 827, 812, 777, 687 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{30}O_3Si$: M^+, 310.1964. Found: *m/z* 310.1959.

(*Z*)-3-Diethoxymethyl-2-methylundec-2-ene-4-ynal (24'hd). A pale yellow oil, R_f



0.43 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 5.21 (s, 1H), 3.78–3.66 (m, 2H), 3.65–3.53 (m, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.90 (s, 3H), 1.59 (quint, *J* = 7.2 Hz, 2H), 1.44–1.19 (m, 6H), 1.26 (t, *J* = 7.0 Hz, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 142.0, 139.4, 103.9, 99.2, 74.7, 62.6, 31.4, 28.7, 28.5, 22.6, 20.1, 15.3, 14.2, 10.7; IR (neat) 2930, 2859, 2214, 1678, 1597, 1454, 1379, 1343, 1329, 1302, 1204, 1123, 1061, 1011, 731 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{28}NO_3$: M^+, 280.2038. Found: *m/z* 280.2033.

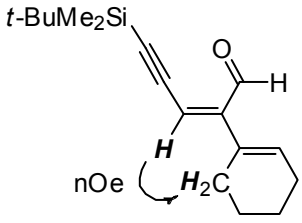
(*Z*)-3-(3-*tert*-Butyldimethylsilyl-2-propyn-1-ylidene)nonanal (24ae). An yellow oil,



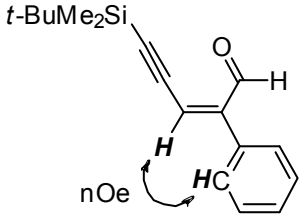
R_f 0.40 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 6.51 (t, *J* = 1.2 Hz, 1H), 2.24 (td, *J* = 7.6, 1.2 Hz, 2H), 1.47–1.20 (m, 8H), 0.97 (s, 9H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ

191.8, 151.1, 125.1, 105.2, 99.6, 31.6, 29.1, 29.0, 28.3, 26.2, 22.7, 16.8, 14.2, –4.6; IR (neat) 2955, 2930, 2858, 1688, 1470, 1250, 1115, 1072, 839, 826, 812, 777, 691 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{30}OSi$: M^+, 278.2066. Found: *m/z* 278.2070.

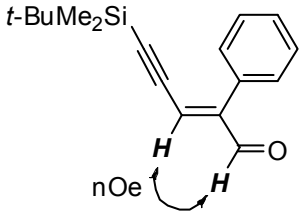
(*Z*)-5-*tert*-Butyldimethylsilyl-2-(cyclohex-1-en-1-yl)pent-2-en-4-ynal (24ai). A pale yellow oil, R_f 0.38 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.4 (s, 1H), 6.52 (s, 1H), 6.42–6.37 (m, 1H), 2.22–2.08 (m, 4H), 1.74–1.55 (m, 4H), 0.97 (s, 9H), 0.17 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 149.5, 131.5, 131.2, 122.2, 107.2, 100.6, 26.7, 26.2, 26.0, 22.6, 21.8, 16.8, –4.6; IR (neat) 2930, 2858, 2129, 1697, 1620, 1470, 1462, 1304, 1250, 1096, 1078, 1007, 839, 826, 812, 777, 683 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{26}OSi$: M^+, 271.1756. Found: *m/z* 271.1743.



(*Z*)-5-*tert*-Butyldimethylsilyl-2-phenylpent-2-en-4-ynal [(*Z*)-24ak]. A pale yellow oil, R_f 0.40 (hexane–ethyl acetate = 30 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.5 (s, 1H), 7.43–7.35 (m, 5H), 6.86 (s, 1H), 1.01 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 148.6, 133.6, 128.9, 128.3, 128.0, 126.8, 108.4, 99.8, 26.2, 16.9, –4.7; IR (neat) 2953, 2930, 2885, 2856, 1692, 1493, 1470, 1464, 1447, 1391, 1362, 1327, 1310, 1250, 1101, 1040, 1016, 939, 880, 839, 826, 812, 777, 764, 746, 694, 633 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{22}OSi$: M^+, 270.1440. Found: *m/z* 270.1438.

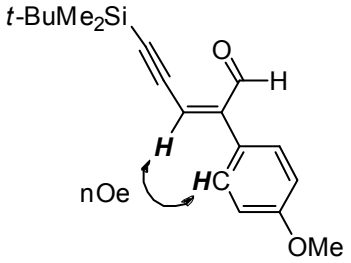


(*E*)-5-*tert*-Butyldimethylsilyl-2-phenylpent-2-en-4-ynal [(*E*)-24ak]. A pale yellow oil, R_f 0.22 (hexane–ethyl acetate = 30 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.58–7.52 (m, 2H), 7.43–7.33 (m, 3H), 6.53 (s, 1H), 0.89 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 148.9, 131.5, 129.2, 128.8, 128.4, 127.8, 112.8, 101.6, 26.1, 16.8, –4.9; IR (neat) 3057, 2953, 2928, 2885, 2856, 2714, 2120, 1693, 1587, 1570, 1497, 1470, 1461, 1445, 1406, 1367, 1250, 1204, 1082, 1028, 1007, 939, 916, 839, 824, 810, 777, 718, 691 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{22}OSi$: M^+,



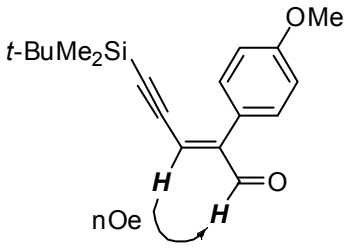
270.1440. Found: *m/z* 270.1442.

(*Z*)-5-*tert*-Butyldimethylsilyl-2-(4-methoxyphenyl)pent-2-en-4-ynal [(*Z*)-24al]. A



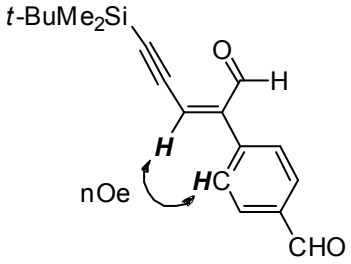
pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.5 (s, 1H), 7.37 (d, *J* = 9.0 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.81 (s, 1H), 3.83 (s, 3H), 1.00 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 160.2, 147.9, 129.2, 126.0, 125.3, 113.8, 107.7, 100.1, 55.3, 26.2, 16.9, –4.6; IR (neat) 2953, 2930, 2889, 2856, 2139, 1688, 1607, 1510, 1470, 1462, 1329, 1308, 1290, 1250, 1180, 1101, 1040, 1020, 1005, 826, 812, 777, 683, 621 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{24}O_2Si$: M^+, 300.1546. Found: *m/z* 300.1556.

(*E*)-5-*tert*-Butyldimethylsilyl-2-(4-methoxyphenyl)pent-2-en-4-ynal [(*E*)-24al]. A



pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.45 (s, 1H), 3.84 (s, 3H), 0.92 (s, 9H), 0.14 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 159.9, 148.0, 130.7, 127.2, 123.7, 113.2, 112.4, 101.9, 55.3, 26.1, 16.8, –4.8; IR (neat) 2953, 2930, 2885, 2856, 2714, 2118, 1693, 1607, 1585, 1568, 1512, 1470, 1462, 1443, 1408, 1369, 1294, 1252, 1207, 1180, 1086, 1032, 1007, 939, 837, 826, 810, 777, 756, 708, 683, 669, 637, 615 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{24}O_2Si$: M^+, 300.1546. Found: *m/z* 300.1559.

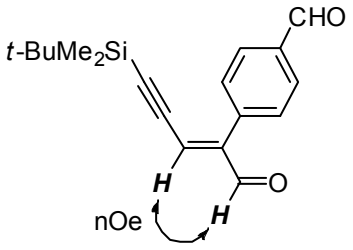
(*Z*)-5-*tert*-Butyldimethylsilyl-2-(4-formylphenyl)pent-2-en-4-ynal [(*Z*)-24am]. A



yellow solid, mp 45.3–46.3 °C, R_f 0.20 (hexane–ethyl acetate = 30 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.5 (s, 1H), 10.0 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 6.95 (s, 1H), 1.00 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.4, 190.0, 147.3, 139.5, 136.2, 129.5, 128.6, 128.5, 110.5, 99.3, 26.2, 16.9, –4.7; IR (KBr) 2953, 2930, 2891, 2856, 2741, 1703, 1692, 1605, 1578, 1562, 1470, 1462, 1391, 1362, 1327, 1310, 1252, 1211,

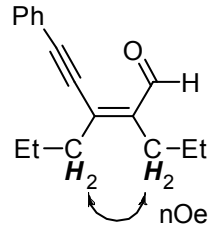
1173, 1103, 1024, 1013, 939, 839, 826, 812, 779, 737, 683 cm^{-1}; HRMS (EI) Calcd for $C_{18}H_{22}O_2Si$: M^+, 298.1389. Found: *m/z* 298.1376.

(*E*)-5-*tert*-Butyldimethylsilyl-2-(4-formylphenyl)pent-2-en-4-ynal [(*E*)-24am]. A



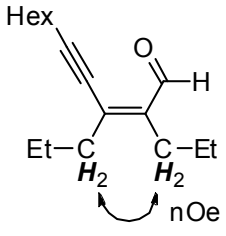
pale yellow oil, R_f 0.15 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.0 (s, 1H), 9.68 (s, 1H), 7.91 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 6.64 (s, 1H), 0.87 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.9, 191.6, 147.8, 137.6, 136.1, 130.2, 130.0, 129.1, 114.9, 100.9, 26.0, 16.8, –4.9; IR (neat) 2953, 2930, 2886, 2857, 2735, 1703, 1697, 1694, 1682, 1609, 1587, 1564, 1506, 1470, 1464, 1408, 1387, 1366, 1308, 1252, 1209, 1171, 1082, 1007, 939, 841, 826, 812, 777, 754, 719, 700, 683, 613 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{13}O_2Si$: $[M–(t\text{-Bu})]^+$, 241.0685. Found: *m/z* 241.0685.

(*Z*)-3-Phenylethynyl-2propylhex-2-en-4-ynal (24da). An yellow oil, R_f 0.53



(hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.4 (s, 1H), 7.55–7.44 (m, 2H), 7.40–7.32 (m, 3H), 2.48 (t, *J* = 7.7 Hz, 2H), 2.33 (t, *J* = 7.8 Hz, 2H), 1.76 (sext, *J* = 7.5 Hz, 2H), 1.39 (sext, *J* = 7.6 Hz, 2H), 1.03 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.8, 145.5, 142.9, 131.6, 129.1, 128.5, 122.4, 99.7, 86.3, 35.9, 27.0, 22.4, 21.5, 14.2, 13.9; IR (neat) 2963, 2932, 2872, 2195, 1672, 1599, 1578, 1489, 1458, 1443, 1256, 1225, 1138, 756, 691 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{20}O$: M^+, 240.1514. Found: *m/z* 240.1517.

(*Z*)-2,3-Dipropylundec-2-en-4-ynal (24ha). An yellow oil, R_f 0.58 (hexane–ethyl

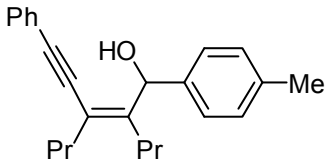


acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 10.2 (s, 1H), 2.41 (t, *J* = 7.0 Hz, 2H), 2.36 (t, *J* = 7.6 Hz, 2H), 2.26 (t, *J* = 7.9 Hz, 2H), 1.67 (sext, *J* = 7.5 Hz, 2H), 1.57 (quint, *J* = 7.7 Hz, 2H), 1.48–1.24 (m, 8H), 0.98 (t, *J* = 7.4 Hz, 3H), 0.95–0.87 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.0, 144.4, 143.9, 101.7, 77.7, 36.4, 31.4, 28.7, 28.6, 26.9, 22.6, 22.5, 21.5, 19.8, 14.3, 14.2, 14.0; IR (neat) 2961, 2932, 2872, 2210,

1674, 1587, 1464, 1381, 1227, 1194, 1113, 1090 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{28}O$: M^+, 248.2140. Found: *m/z* 248.2135.

Reaction of 24da with a *p*-tolyl Grignard reagent

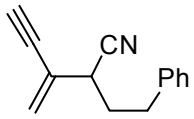
A solution of *p*-tolylmagnesium bromide in diethyl ether (ca. 1.20 mmol) was added to a solution of **24da** (96 mg, 0.40 mmol) in diethyl ether (2.0 mL) at 0 °C, and the resulting mixture was stirred at 0 °C for 2 h before quenching with a saturated NH_4Cl aqueous solution. The organic layer was separated, and the aqueous layer was extracted with diethyl ether. The combined organic layer was washed with a saturated NH_4Cl aqueous solution and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate = 10 : 1 as an eluent) to give (*Z*)-3-phenylethynyl-2-propyl-1-*p*-tolylpent-2-en-1-ol[11d] (**25**, 110 mg, 83%) as an yellow oil, R_f 0.13 (hexane–ethyl acetate = 20 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.36–7.27 (m, 3H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.29 (s, 1H), 2.36 (s, 3H), 2.27 (t, *J* = 7.6 Hz, 2H), 2.20–1.97 (m,3H), 1.72 (sext, *J* = 7.5 Hz, 2H), 1.48–1.32 (m, 1H), 1.20–1.05 (m, 1H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.86 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 139.6, 136.5, 131.3, 128.8, 128.3, 127.9, 125.3, 123.6, 120.8, 93.4, 89.3, 75.2, 34.0, 29.8, 23.8, 21.8, 21.1, 14.8, 13.9; IR (neat) 2959, 2930, 2870, 1504, 1495, 1454, 1111, 1034, 818, 754, 691 cm^{-1}.



Desilylation of 15b

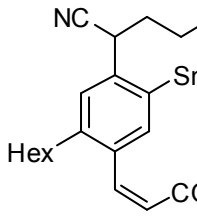
To a solution of **15b** (0.43 g, 1.40 mmol) in THF (28 mL) were added AcOH (0.23 g, 3.8 mmol) and a 1.0 M solution of TBAF (2.8 mL, 2.8 mmol) in THF successively at 0 °C. The resulting reaction mixture was warmed up at room temperature and further stirred for 1 h before quenching with water. The aqueous layer was extracted three times with diethyl ether. The combined organic layer was washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate = 40:1 as an

eluent) to give 3-methylene-2-(2-phenylethyl)-pent-4-ynenitrile (**26**, 0.21 g, 77%) as a pale yellow oil, R_f 0.44 (hexane–ethyl acetate = 5 : 1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 2H), 7.27–7.19 (m, 3H), 5.72 (d, *J* = 0.73 Hz, 1H), 5.71 (s, 1H), 3.31 (t, *J* = 7.1 Hz, 1H), 3.06 (s, 1H), 2.90–2.73 (m, 2H), 2.28–2.13 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5, 128.5, 128.3, 126.4, 125.9, 125.0, 118.6, 80.2, 80.1, 37.4, 33.3, 32.6; IR (neat) 3285, 3028, 2930, 2864, 2243, 1616, 1603, 1497, 1454, 1030, 922, 750, 700 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{13}N$: M^+, 195.1048. Found: *m/z* 195.1046.



Stannylative cross-cyclodimerization of 26 with ethyl (*Z*)-2-undecen-4-ynoate (27).

To a solution of Cp(allyl)Pd (1.06 mg, 5.0 μmol) in THF (0.60 mL) were added *N*-(2-diphenylphosphinobenzylidene)cyclohexylamine (**28**) (3.7 mg, 10.0 μmol), $(Bu_3Sn)_2O$ (60 mg, 0.100 mmol), **26** (59 mg, 0.30 mmol), and ethyl (*Z*)-2-undecen-4-ynoate (**27**) (63 mg, 0.30 mmol) sequentially. The resulting mixture was stirred at 50 °C for 24 h, filtered through a Florisil pad, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexane–ethyl acetate = 30:1 with 0.2% Et_3N as an eluent) followed by preparative GPC gave ethyl (*Z*)-3-(2-hexyl-4-(1-cyano-3-phenylprop-1-yl)-5-(tributylstannyl)phenyl-2-propenoate (**29**, 74 mg, 53%) as a pale yellow oil, R_f 0.30 (hexane–ethyl acetate = 20 : 1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.20 (m, 7H), 7.15 (d, *J* = 11.7 Hz, 1H), 6.03 (d, *J* = 12.1 Hz, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 3.53 (dd, *J* = 11.0, 4.9 Hz, 1H), 3.08–2.96 (m, 1H), 2.92–2.80 (m, 1H), 2.59 (t, *J* = 7.9 Hz, 2H), 2.32–2.18 (m, 1H), 2.10–1.96 (m, 1H), 1.62–1.24 (m, 20H), 1.09 (t, *J* = 7.1 Hz, 3H), 0.98–0.86 (m, 18H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 143.0, 142.3, 141.5, 139.6, 137.6, 137.3, 134.1, 128.6, 128.4, 127.2, 126.4, 121.6, 120.9, 60.0, 39.5, 38.4, 33.9, 33.8, 31.7, 30.6, 29.3, 29.1, 27.4, 22.7, 14.2, 14.1, 13.7, 10.5; IR (neat): 2957, 2928, 2870, 2855, 2239, 1726, 1634, 1589, 1464, 1456, 1416, 1377, 1173, 1032, 908 cm^{-1}; HRMS (EI) Calcd for $C_{35}H_{50}NO_2Sn$: $[M–Bu]^+$, 636.2864. Found: *m/z* 636.2859.



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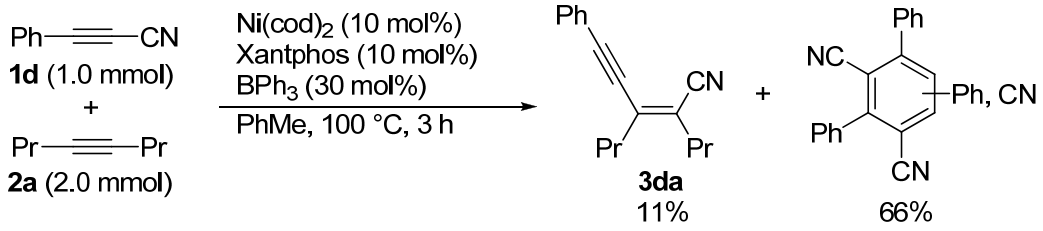

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Chapter 4

Nickel/Lewis Acid-Catalyzed Cyanoesterification and Cyanocarbamoylation of Alkynes

Cyanoformates and cyanoformamides are found to add across alkynes upon catalysis by nickel/Lewis acid to give β-cyano-substituted acrylates and acrylamides, respectively, in highly stereoselective and regioselective manners. The resulting adducts serve as versatile synthetic building blocks through chemoselective transformation of the ester, amide, and cyano groups as demonstrated by synthesis of typical structures of β-cyano ester, β-amino nitrile, γ-lactam, di-substituted maleic anhydride, and γ-aminobutyric acid. Cyanoformate thioester and benzoyl cyanide, on the other hand, are disclosed to undergo decarbonylative addition across alkynes in the presence of palladium/Lewis acid catalysts.

Introduction

Vicinal difunctionalization of alkynes with carbonaceous groups through direct cleavage of C–C bonds followed by insertion of alkynes has gained much interest in organic synthesis, mainly because the transformation allows simultaneous construction of two different carbon–carbon bonds.[1–3] In this regard, nickel or nickel/Lewis acid-catalyzed addition reactions of nitriles across alkynes, namely carbocyanation reaction, have been demonstrated as a new protocol of this class of transformations.[4–9] Various nitriles such as aryl,[4,6] allyl,[5] alkenyl,[6] alkynyl,[7] and alkyl cyanides[6,8] participate in the reaction to give highly substituted acrylonitriles with good stereo- and regioselectivities. Nitriles having carbonyl–CN bonds also add across arylethynes,[9] norbornene,[10] and 1,2-dienes[11] with palladium and nickel catalysts. Intermolecular addition reaction of benzoyl cyanide across arylethynes results in benzoylation of the terminal alkyne carbon followed by hydrocyanation of the resulting alkynyl ketones and isomerization of the double bond, making the reaction scope extremely limited.[9] Cyanocarbamoylation of alkynes and alkenes recently reported by Takemoto proceeds only intramolecularly.[12] Accordingly, intermolecular addition reactions of such nitriles across alkynes with a general substrate scope remain unexplored, and their development is highly desired as a new tool to introduce two different functional groups at a vicinal position with defined stereochemistry. Described in this Chapter are nickel/Lewis acid-catalyzed cyanoesterification and cyanocarbamoylation reactions of alkynes to give *β*-cyano-substituted acrylate esters and acrylamides stereo- and regioselectively. Subsequent transformations of the two functional groups thus introduced are demonstrated to readily afford a range of building blocks including *β*-cyano ester, *β*-amino nitrile, *γ*-lactam, di-substituted maleic anhydride, and *γ*-aminobutyric acid. Also described is that cyanoformate thioesters and cyano ketones react with alkynes under decarbonylation especially with the aid of palladium/Lewis acid-catalysts.

Results and discussion

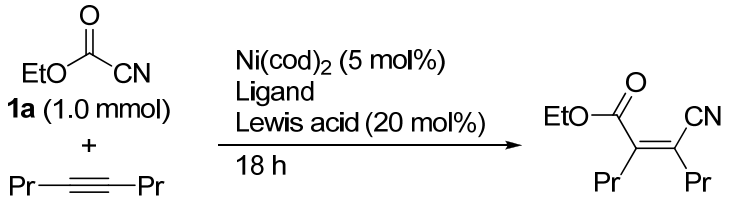
Nickel/BAr_3-catalyzed cyanoesterification of alkynes

The author first examined the reaction of ethyl cyanoformate (**1a**) with 4-octyne (**2a**) at 100 °C in the presence of a nickel catalyst along with various ligands and Lewis

acid cocatalysts (Table 1). PMe_2Ph and PMe_3, ligands of choice for cyanoesterification of 1,2-dienes[11] and arylcyanation of alkynes,[4] respectively, were completely ineffective (entries 1 and 2). Among triarylphosphines examined (entries 3–6), electron-deficient ones such as $P(4\text{-}CF_3\text{–}C_6H_4)_3$ and $P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ gave a small amount of desired adduct **3aa** (entries 3 and 4). Encouraged by these observations, he examined the effect of Lewis acid cocatalysts. Of Lewis acids examined with $P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ as a lignad (entries 7–10), $B(C_6F_5)_3$ was found to be effective to give **3aa** in 64% yield as estimated by GC (entry 10). The reaction proceeded even at 35 °C in a higher yield of **3aa** (entry 11). A slight increase in yield of **3aa** was further observed using 20 mol% of the ligand, and the reaction with a 1.00 mmol scale for 24 h gave **3aa** in an 80% isolated yield (entry 12). Use of more polar solvents such as 1,4-dioxane and DMF was not effective, probably because they acted as a Lewis base to coordinate to Lewis acid cocatalyst $B(C_6F_5)_3$ (entries 13 and 14).

With the optimized conditions in hand, the author next studied the scope of alkynes using **1a** (Table 2). The addition across 1,4-bis(trimethylsilyl)-2-butyne (**2b**) yielded highly functionalized allylsilane **3ab** stereoselectively in 75% yield (entry 1). The stereochemistry of **3ab** was confirmed by nOe observed between two allylic methylenes. An unsymmetrical alkyne, 4,4-dimethyl-2-pentyne (**2d**), gave the corresponding adduct **3ad** with complete regioselectivity (entry 3), whereas 4-methyl-4-pentyne (**2c**) gave a mixture of regioisomers (entry 2). The regioselectivities are identical to that observed for the carbocyanation reactions of alkynes with other nitriles:[4–8] isomers having a larger substituent at the cyano-substituted carbon were produced preferentially. On the other hand, **1a** reacted with silyl-substituted alkynes highly stereo- and chemoselectively but with opposite regioselectivity using BPh_3 as a Lewis acid in 1,4-dioxane instead of $B(C_6F_5)_3$ in toluene (entries 4–11). The use of $B(C_6F_5)_3$ for the reaction of **1a** and **2e** in toluene gave **3ae** in only 17% yield. Methyl cyanoformate (**1b**) also added across **2f** in a moderate yield under the similar conditions (entry 6).

Table 1. Cyanoesterification of 4-octyne (**2a**) using ethyl cyanoformate (**1a**).[a]



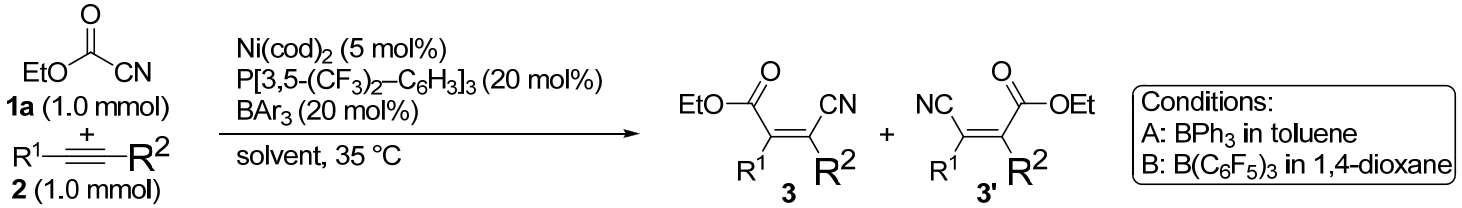
Entry	Ligand (mol%)	Lewis acid	Solvent	Temp. (°C)	Yield (%)[b]
1	PMe_3 (10)	none	toluene	100	0
2	PMe_2Ph (10)	none	toluene	100	0
3	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	none	toluene	100	4
4	$P(4\text{-}CF_3\text{–}C_6H_4)_3$ (10)	none	toluene	100	4
5	PPh_3 (10)	none	toluene	100	0
6	$P(4\text{-}MeO\text{–}C_6H_4)_3$ (10)	none	toluene	100	0
7	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	$AlMe_3$	toluene	100	0
8	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	$AlMe_2Cl$	toluene	100	0
9	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	BPh_3	toluene	100	35
10	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	$B(C_6F_5)_3$	toluene	100	64
11	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (10)	$B(C_6F_5)_3$	toluene	35	74
12	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (20)	$B(C_6F_5)_3$	toluene	35	83 (80)[c]
13	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (20)	$B(C_6F_5)_3$	1,4-dioxane	35	42
14	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (20)	$B(C_6F_5)_3$	DMF	35	0

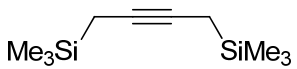
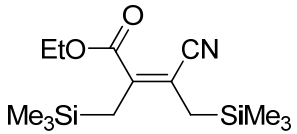
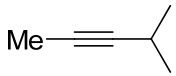
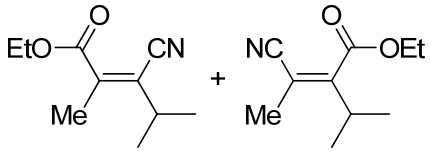
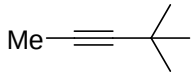
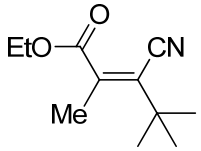
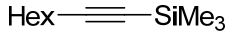
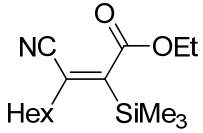
[a] All the reaction was carried out using **1a** (0.20 mmol), **2a** (0.20 mmol), $Ni(cod)_2$ (10.0 μmol), a ligand (20 or 40 μmol), and a Lewis acid (40 μmol) in toluene (0.133 mL). [b] Estimated by GC using tridecane as an internal standard. [c] Isolated yield with a 1.00 mmol scale.

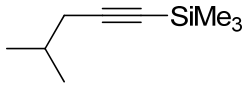
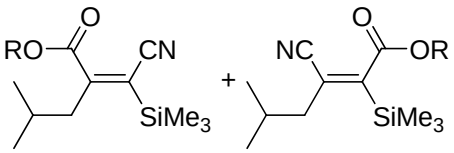
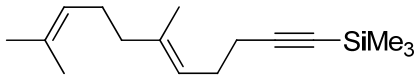
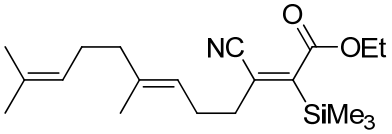
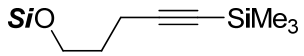
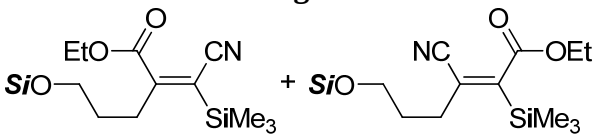
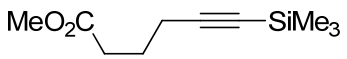
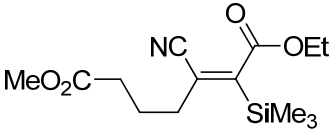
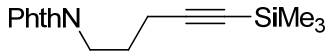
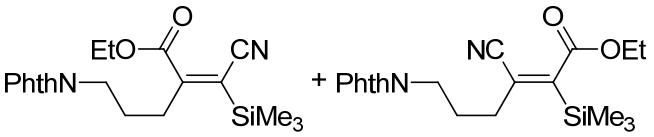
The reaction likely proceeds through a catalytic cycle shown in Scheme 1. The cycle should be initiated by oxidative addition of C–CN bonds of cyanoformate esters[13] by the aid of BAr_3 to give **4**. After the phosphine ligand in **4** was replaced by an alkyne to give **5** or **6**, the alkoxycarbonyl group migrates to the less hindered carbon of the coordinating alkyne, and **7** or **8** results, whose reductive elimination followed by transfer of BAr_3 to **1** gives adduct **3** or **3'** and regenerate nickel(0) and a BAr_3 adduct of **1**. Although an attempt failed to isolate an oxidative adduct from **1a**, $Ni(cod)_2$, and Lewis acid with various phosphine ligands, the cyano group rather than the ester carbonyl is considered to coordinate to the borane Lewis acid throughout the catalytic cycle, making the cyano group less nucleophilic to undergo the migratory insertion. It is known that M–CN bond cleavage requires high temperature.[14] Treatment of ethyl cyanoformate (**1a**) with $B(C_6F_5)_3$ in C_6D_6 showed upfield shifts of ^{13}C NMR signals for

the cyano (110.6 ppm to 104.5 ppm) and the carbonyl (144.7 ppm to 141.6 ppm) groups (eq. 1).[15] On the other hand, IR spectra showed upwavenumber shifts for the cyano (2247 cm^{-1} to 2398 cm^{-1}) and downwavenumber shifts for the carbonyl (1747 cm^{-1} to 1649 cm^{-1}). These data would support the coordination of the cyano group to BAr_3.[16] Alkenylnickel intermediate **7** looks kinetically favored since the migration of the alkoxycarbonyl group to the less hindered carbon of the coordinating alkyne in **5** should proceed in a manner similar to other carbocyanation reactions of alkynes.[4–8] With silyl-substituted alkynes, on the other hand, an electron-donating nature of a silyl group might reverse regioselectivity of the migratory insertion step, making the carbon α to a silyl group less electron-rich to favor nucleophilic migration of the alkoxycarbonyl group. Alternatively, alkenylnickel **7** might be reluctant to reductive elimination due to bulkiness and it could isomerize to **8** via β-carbon elimination through **5**. Then isomerization to **6** gives **3'** finally upon reductive elimination from **8**. Ratios of **3**:**3'** were constant during the reactions of silyl-substituted alkynes, suggesting that **3'** should be kinetic products and the irreversibility of the reductive elimination. Lower regioselectiviy observed in the reaction of **1a** with **2e** at 80 °C (20% yield, **3ae**/**3'ae** = 30 : 70, cf. entry 4 of Table 2) could be ascribed to acceleration of the reductive elimination from **7** before such reversible processes involving β-carbon elimination. On the other hand, no loss of regioselectivity was observed in the reaction of **1a** with **2d**: **3ad** was produced as a single isomer in 55% yield even at 80 °C (cf. entry 3 of Table 2), suggesting that reductive elimination from **7** with an alkyl substitutent for R^3 would be fast enough.

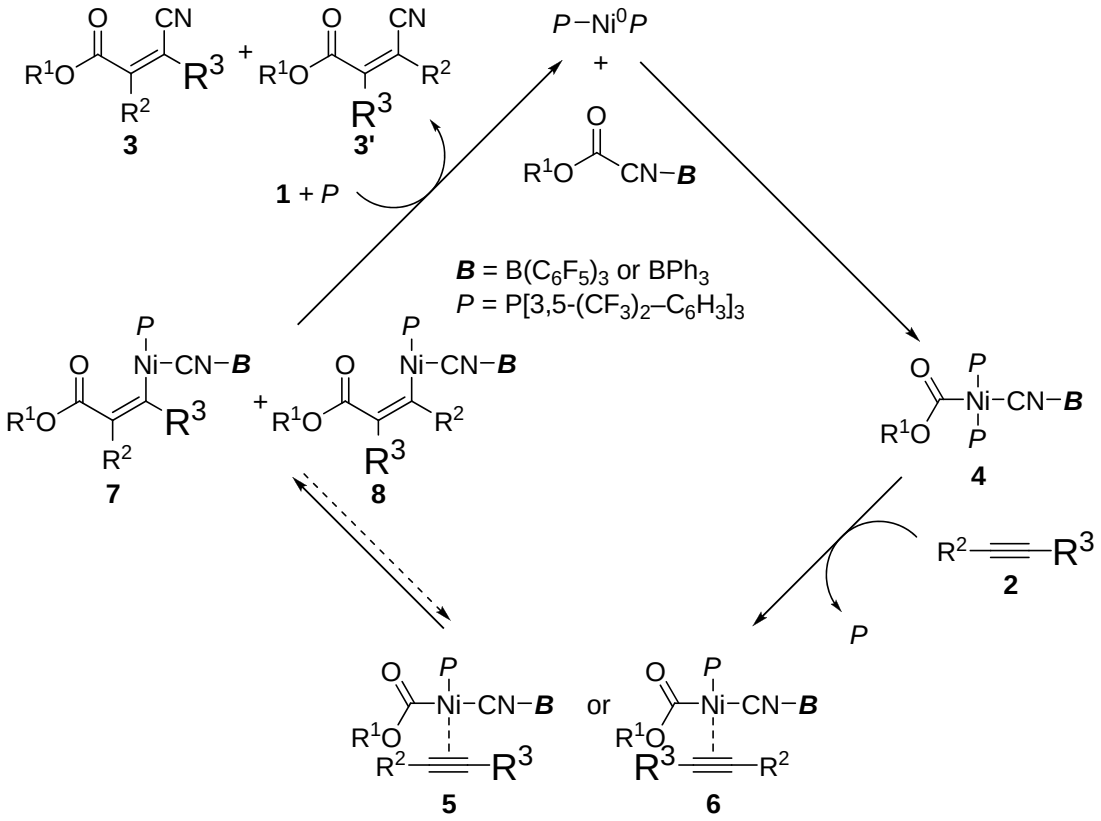
Table 2. Nickel/BAr_3-catalyzed cyanoesterification of alkynes.[a]



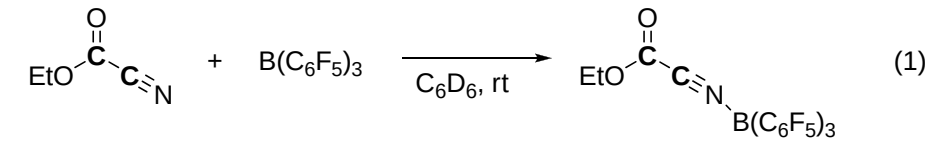
Entry	Alkyne	Cond.	Time (h)	Product(s)	Yield (%)[b] **3**:**3'**[c]
1	 **2b**	A	21	 **3ab**	75
2	 **2c**	A	46	 **3ac** **3'ac**	35 (53:47)
3	 **2d**	A	46	 **3ad**	49 (>99:1)
4	 **2e**	B	22	 **3'ae**	75 (1:>99)

5	 **2f**	B	16	 **3af** (R = Et) **3bf** (R = Me) **3'af** (R = Et) **3'bf** (R = Me)	85 (6:94)
6[d]		B	24		59 (7:93)[e]
7	 **2g**	B	22	 **3'ag**	64 (1:>99)
8	 ***Si*** = $SiMe_2t$-Bu **2h**	B	46	 **3ah** **3'ah**	67 (1:99)[e]
9	 **2i**	B	41	 **3'ai**	62 (1:>99)
10	 **2j**	B	51	 **3aj** **3'aj**	67 (3:97)

[a] All the reaction was carried out using **1a** (1.00 mmol), an alkyne (1.00 mmol), $Ni(cod)_2$ (50 μmol), a ligand (0.100 or 0.20 mmol), and a Lewis acid (0.20 mmol) in solvent (0.67 mL). [b] Isolated yield. [c] Estimated by ^1H NMR analysis of an isolated product. [d] Methyl cyanoformate (**1b**) was used instead of **1a**.[e] Calculated based on yields of isolated products.



Scheme 1. Plausible mechanism of cyanoesterification of alkynes.



^{13}C NMR
δ_{CO}: 144.7 ppm
δ_{CN}: 110.6 ppm

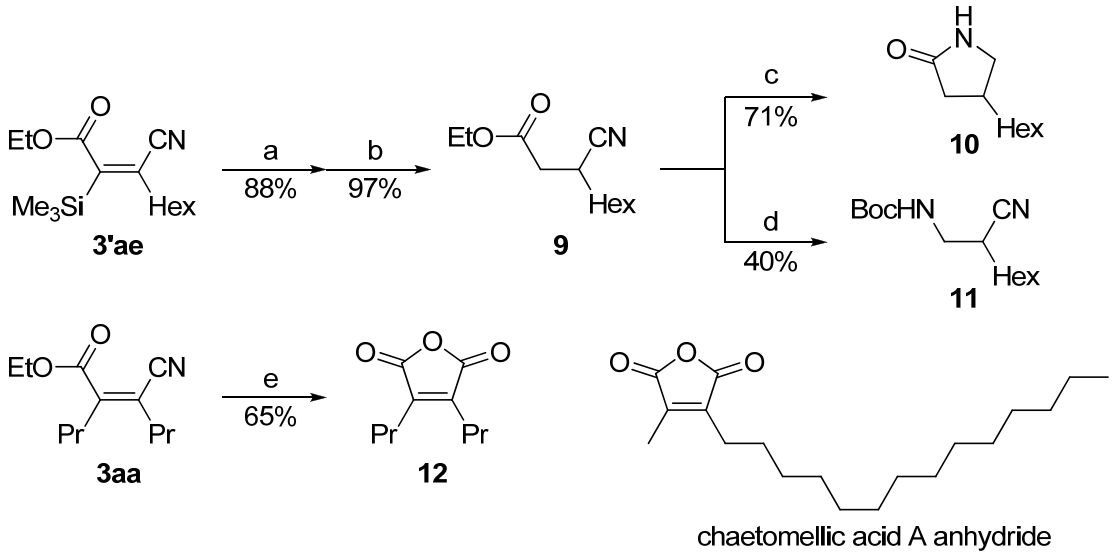
IR (neat)
υ_{CO}: 1747 cm^{-1}
υ_{CN}: 2247 cm^{-1}

^{13}C NMR
δ_{CO}: 141.6 ppm
δ_{CN}: 104.5 ppm

IR (KBr)
υ_{CO}: 1649 cm^{-1}
υ_{CN}: 2398 cm^{-1}

Synthetic versatility of the cyanoesterification products is demonstrated by the transformations shown in Scheme 2. Protodesilylation followed by reduction of the remaining double bond gave β-cyano ester **9**. Upon treatment of **9** with $NaBH_4$ in the presence of $CoCl_2$, γ-lactam **10** was obtained,[17] whereas hydrolysis of the ester group[18] in **9** and the subsequent Curtius rearrangement[19] afforded *N*-Boc-protected β-cyano amide **11**, a potential precursor for β-amino acid derivatives.[20] On the other hand,

di-substituted maleic anhydride **12** was obtained upon treatment of **3aa** with a base. Di-substituted maleic anhydrides are found in many natural products such as chaetomellic acid A anhydride,[21] and the present protocol would be applicable to the synthesis of the class of compounds starting with readily available cyanoformate esters and internal alkynes.



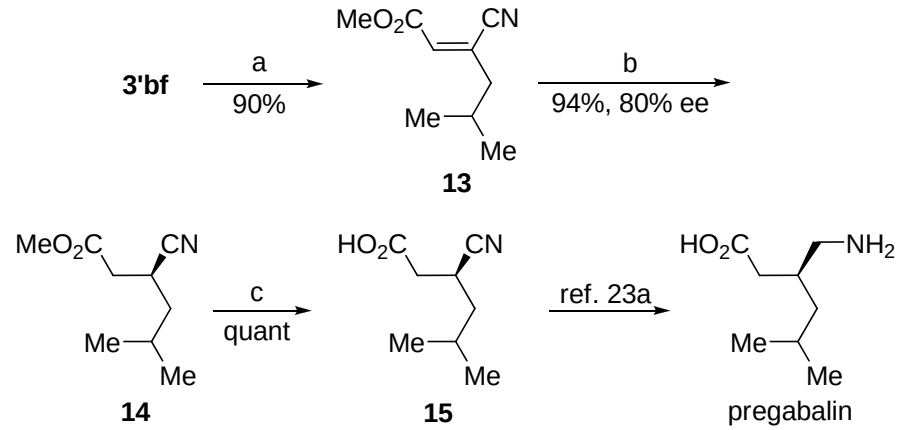
Reagents and Conditions: (a) TBAF, CF_3CO_2H, THF, 0 °C, 1.5 h; (b) H_2, Pd/C (10 mol%), dioxane, rt, 2.5 h; (c) $CoCl_2$, $NaBH_4$, EtOH, 0 °C to rt, 11 h; (d) $Ba(OH)_2 \cdot H_2O$, MeOH, rt, 4 h, then $Ph_2P(O)N_3$, NEt_3, *t*-BuOH, 75 °C, 11 h; (e) NaOH, EtOH, H_2O, 80 °C, 20 h.

Scheme 2. Transformations of the cyanoesterification products.

Synthetic potential of the cyanoesterification is also demonstrated by formal synthesis of pregabalin, an anticonvulsant drug used for treatment of neuropathic pain (Scheme 3).[22,23] Protodesilylation of **3'bf** followed by enantioselective conjugate reduction of the α,β-unsaturated ester moiety with PMHS (polymethylhydrosiloxane) and a chiral Cu/(*R*)-binap catalyst[24] afforded β-cyano ester **14** of 80% ee, which was hydrolyzed to give a precursor of pregabalin **15**.[22a]

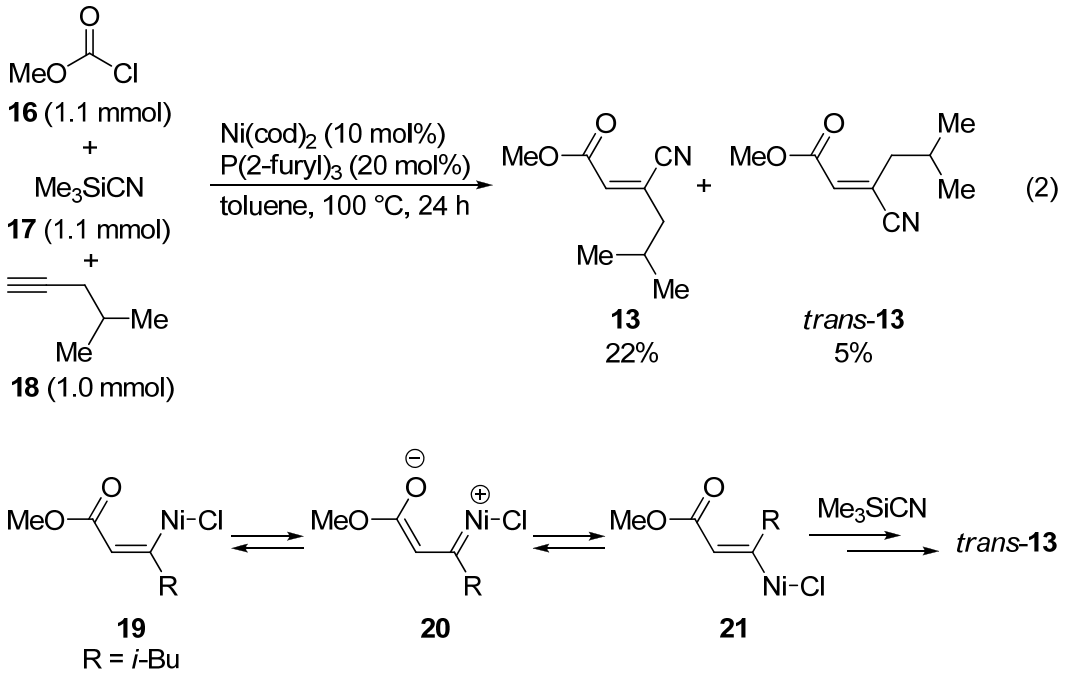
The author also found that β-cyanoacrylates such as **13** could be obtained as a mixture of stereoisomers by three-component coupling reaction of chloroformate esters, silyl cyanides, and terminal alkynes by a nickel/P(2-furyl)$_3$ catalyst, although the yield was modest (eq. 2). The isomer ratio was roughly constant during the reaction,

suggesting that the *trans*-adduct would be derived from isomerization of alkenylnickel intermediate **19** to **21** through **20** due to slow transmetalation with trimethylsilyl cyanide (Scheme 4).



Reagents and Conditions: (a) TBAF, CF_3CO_2H, THF, 0 °C, 2 h; (b) CuCl (5 mol%), NaO*t*-Bu (5 mol%), (*R*)-BINAP (5 mol%), PMHS, *t*-BuOH, toluene, rt, 24 h; (c) $Ba(OH)_2 \cdot H_2O$, MeOH, rt, 2 h.

Scheme 3. Formal synthesis of pregabalin.



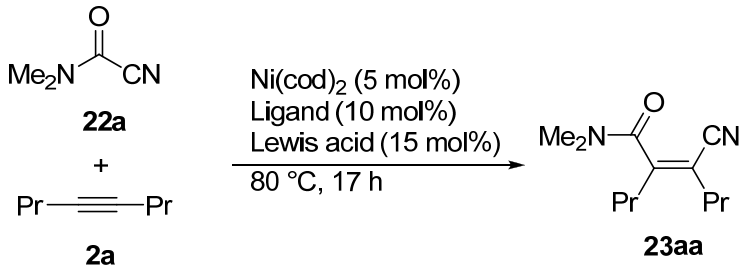
Scheme 4. Formation of stereoisomer *trans*-**13**.

Nickel/BPh_3-catalyzed cyanocarbamoylation of alkynes

The author next turned his attention to the addition reactions of cyanoformamides across alkynes. He first surveyed nickel/Lewis acid catalysts for the reaction of *N*,*N*-dimethylcyanoformamide (**22a**) with 4-octyne (**2a**) (Table 3). Of various combinations of $Ni(cod)_2$, a ligand, and a Lewis acid examined, electron-donating and sterically bulky ligands with BPh_3 as a Lewis acid gave better yields of *β*-cyano-substituted acrylamide **23aa**, and a combination of $Ni(cod)_2$ (5 mol%), $PCyPh_2$ (10 mol%), and BPh_3 (15 mol%) was found optimum to give **23aa** in 93% isolated yield (entry 4). The use of other Lewis acids such as $B(C_6F_5)_3$ and $AlMe_3$ with $PCyPh_2$ completely retarded the reaction (entries 6 and 7), whereas only a trace amount of **23aa** was obtained in the absence of a Lewis acid catalyst (entry 8). Use of 1,4-dioxane as a solvent did not affect the reaction, while Lewis basic DMF retarded the reaction (entries 9 and 10). The catalysts suitable for the cyanoesterification were not effective (entries 12 and 13). No trace amount of the adduct was obtained with $Pd(PPh_3)_4$, a catalyst of choice for the intramolecular cyanocarbamoylation of alkynes.[12]

Cyanoformamides derived from *N*-methylbenzylamine (**22b**) and morpholine (**22c**) also added across **2a** in good yields (entries 1 and 2 of Table 4). Both of two C–CN bonds of piperazin-1,4-dicarbonyl cyanide (**22d**) underwent the addition across two molar equivalents of **2a**, giving double cyanocarbamoylation product **23da**, the structure of which was confirmed by X-ray crystallography (entry 3 and Figure 1). Monocyanocarbamoylation product was not observed due presumably to its solubility higher than that of **22d** in toluene. The reaction of **22a** with 4-methyl-4-pentyne (**2d**) gave **23ad** in poor yield but as a single isomer with regioselectivity opposite to the cyanoesterification (entry 4, cf. entry 2 of Table 2). Reactions with silyl-substituted alkynes also proceeded with excellent stereo, regio-, and chemoselectivities with P*i*-$PrPh_2$ as a ligand in a 1,4-dioxane solvent to afford single isomers (entries 5–10). The observed regioselectivities were similar to those for the cyanoesterification reaction of silyl-substituted alkynes. The structure of the adducts was assigned based on nOe experiments of ^1H NMR for desilylated **23ae**.

Table 3. Cyanocarbamoylation of 4-octyne (**2a**) using *N*,*N*-dimethylcyanoformamide (**22a**).[a]



Entry	Ligand	Lewis acid	Solvent	Yield (%)[b]
1	PMe_3	BPh_3	toluene	17
2	PCy_3	BPh_3	toluene	73
3	PCy_2Ph	BPh_3	toluene	89
4	$PCyPh_2$	BPh_3	toluene	100 (93)[c]
5	P*i*-PrPh_2	BPh_3	toluene	91
6	$PCyPh_2$	$B(C_6F_5)_3$	toluene	0
7	$PCyPh_2$	$AlMe_3$	toluene	0
8	$PCyPh_2$	none	toluene	6
9	$PCyPh_2$	BPh_3	1,4-dioxane	92
10	$PCyPh_2$	BPh_3	DMF	14
11	PPh_3	BPh_3	toluene	60
12	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$	BPh_3	toluene	15
13	$P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$	$B(C_6F_5)_3$	toluene	12

[a] All the reaction was carried out using **22a** (0.20 mmol), **2a** (0.20 mmol), $Ni(cod)_2$ (10.0 μmol), a ligand (20 μmol), and a Lewis Acid (30 μmol) in toluene (0.40 mL). [b] Estimated by GC using tetradecane as an internal standard. [c] Isolated yield obtained with a 1.00 mmol scale reaction.

To gain a mechanistic insight for the cyanocarbamoylation reaction, the author examined the stoichiometric reaction (0.50 mmol scale) of **22a**, $Ni(cod)_2$, two molar equivalents of $PCyPh_2$, and BPh_3 in benzene-d_6. The reaction mixture immediately turned to a homogeneous orange solution at room temperature, and a new nickel species was observed at δ 32.1 (s) in ^{31}P NMR, which was assigned to be *trans*-$(Ph_2CyP)_2Ni(CN)[CO(BPh_3)NMe_2]$ (**24**) (Scheme 5). Evaporation of the solvent *in vacuo* followed by washing of the resulting precipitates with hexane gave the complex as a pale yellow powder in 80% yield. Although attempted recrystallization of **24** was unsuccessful, ^{13}C NMR analyses showed signals at δ 193.4 ppm (t, $J_{C–P}$ = 21.9 Hz) for the carbonyl and at δ 141.9 ppm (t, $J_{C–P}$ = 20.7 Hz) for the cyano group, suggesting that both the aminocarbonyl and cyano groups are bound to the nickel center with two equivalent phosphorus ligands coordinated in *trans* geometry. A related

oxidative adduct of carbamoyl chloride to $Ni(cod)_2/PCyPh_2$ showed a signal at δ 188.5 ppm (t, J_{C-P} = 26.3 Hz) for the carbonyl (eq. 3). On the other hand, related cyanonickel(II) complexes with a cyano group coordinating to a Lewis acid show signals at δ 154.8 ppm for the cyano groups (Figure 2).[25] Based on these data, the aminocarbonyl group appears to BPh_3 in **24**. The resulting oxidative adduct **24** reacted with five molar equivalents of 4-octyne (**2a**) in benzene-d_6 at 60 °C for 1 h to give a new nickel complex showing a signal at δ 45.3 ppm (s) in ^{31}P NMR, and cyanocarbamoylation product **23aa** was also observed in ^{1}H NMR in 40% yield as estimated by GC. The new nickel complex observed was assigned to be **25** based on the same set of peaks observed in the reaction of $Ni(cod)_2$, $PCyPh_2$ (2.0 equiv), and **2a** (5.0 equiv). No conversion of **24** was observed when the reaction was run at room temperature for 24 h, suggesting that coordination of alkynes may be the rate-determining step. Moreover, oxidative adduct **24** served as a catalyst for the reaction of **22a** (0.20 mmol) with **2a** (0.20 mmol) in the presence of BPh_3 (10 mol%) in toluene at 80 °C to give **23aa** in 85% yield after 17 h as estimated by GC. These results clearly suggest that **24** should be a plausible intermediate for the cyanocarbamoylation.

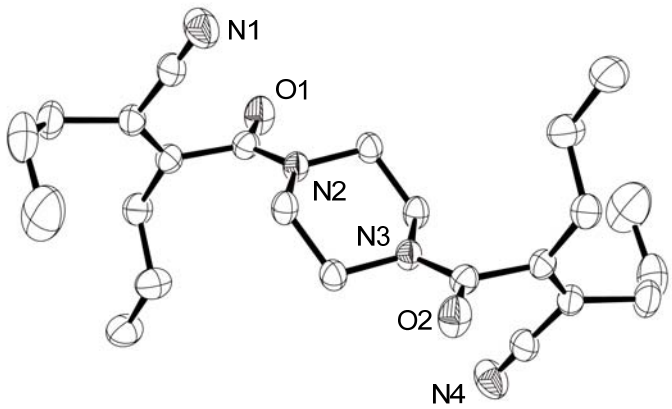
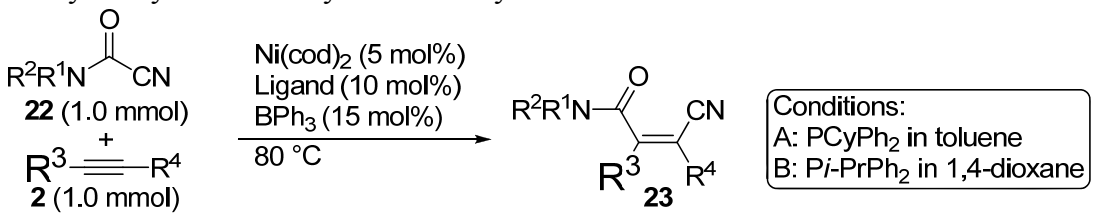
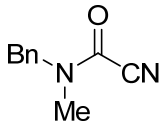
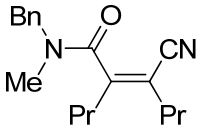
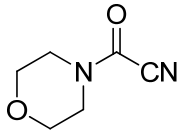
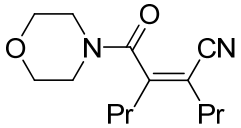
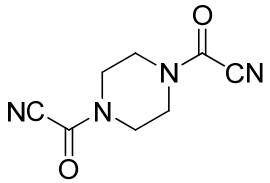
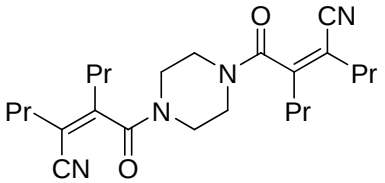
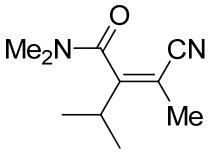


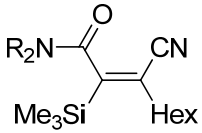
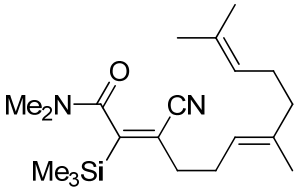
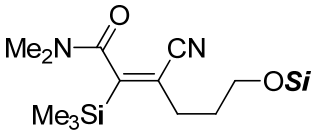
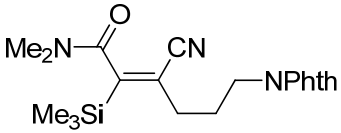
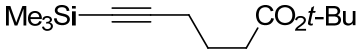
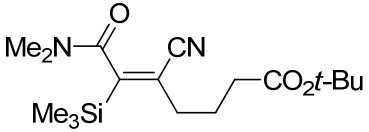
Figure 1. ORTEP drawing of **23da**.

Table 4. Nickel–BPh_3-catalyzed cyanocarbamoylation of alkynes.[a]

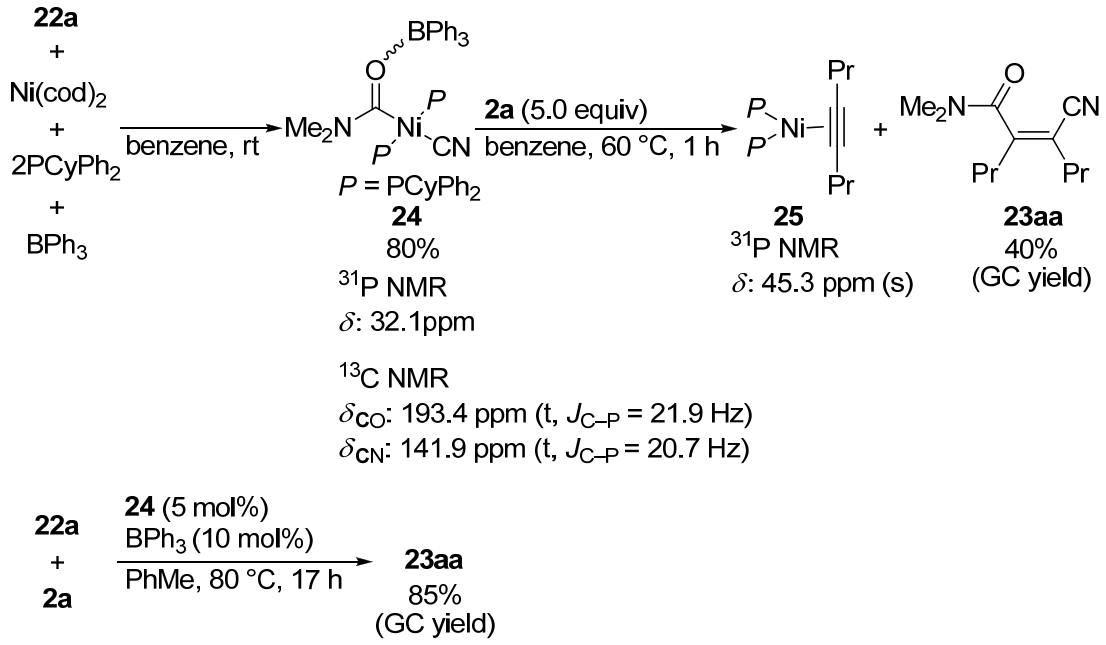


Entry	22	2	Cond	Time (h)	Product	Yield (%)[b]
1	 **22b**	**2a**	A	27	 **23ba**	82
2	 **22c**	**2a**	A	23	 **23ca**	87
3[c]	 **22d**	**2a**	A	70	 **23da**	65[d]
4	**22a**	**2d**	A	24	 **23ad**	31

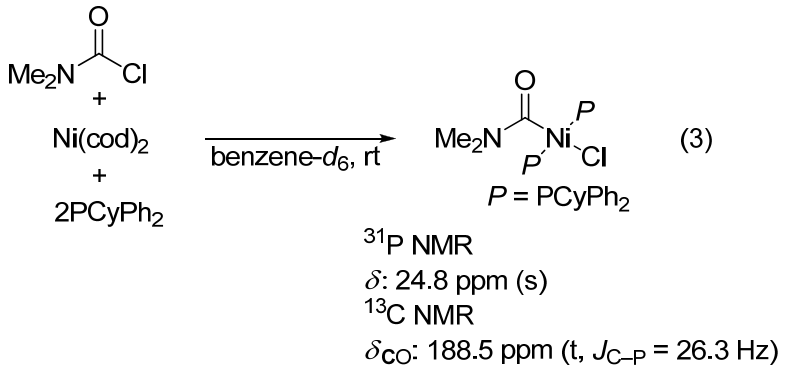
154

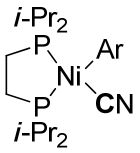
5	**22a**	**2e**	B	22	 **23ae** (R = Me) **23ce** (NR_2 = morpholine)	66
6	**22c**	**2e**	B	22		79
7	**22a**	**2g**	B	41	 **23ag**	56
8	**22a**	**2h**	B	39	 ***Si*** = $SiMe_2t$-Bu **23ah**	66
9	**22a**	**2j**	B	50	 **23aj**	42
10	**22a**	 **2k**	B	41	 **23ak**	62

[a] All the eaction was carried out using **22** (1.00 mmol), alkyne (1.00 mmol), $Ni(cod)_2$ (50 μmol), a ligand (100 μmol), and a Lewis Acid (150 μmol)in solvent (2.0 mL). [b] Isolated yield. [c] 2.0 mmol of **2a** was used. [d] Isolated yield based on **22d**.



Scheme 5. Synthesis and reactions of *trans*-$(Ph_2CyP)_2Ni(CN)[CO(BPh_3)NMe_2]$ (**24**).



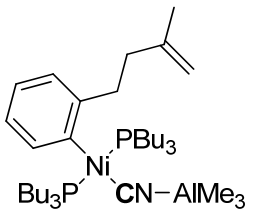


^{13}C NMR

δ_{CN}: 136.3 ppm (dd, J_{C-P} = 75.0, 30.0 Hz), Ar = 2-pyridyl

δ_{CN}: 136.6 ppm (br m), Ar = 3-pyridyl

δ_{CN}: 136.4 ppm (br m), Ar = 4-pyridyl



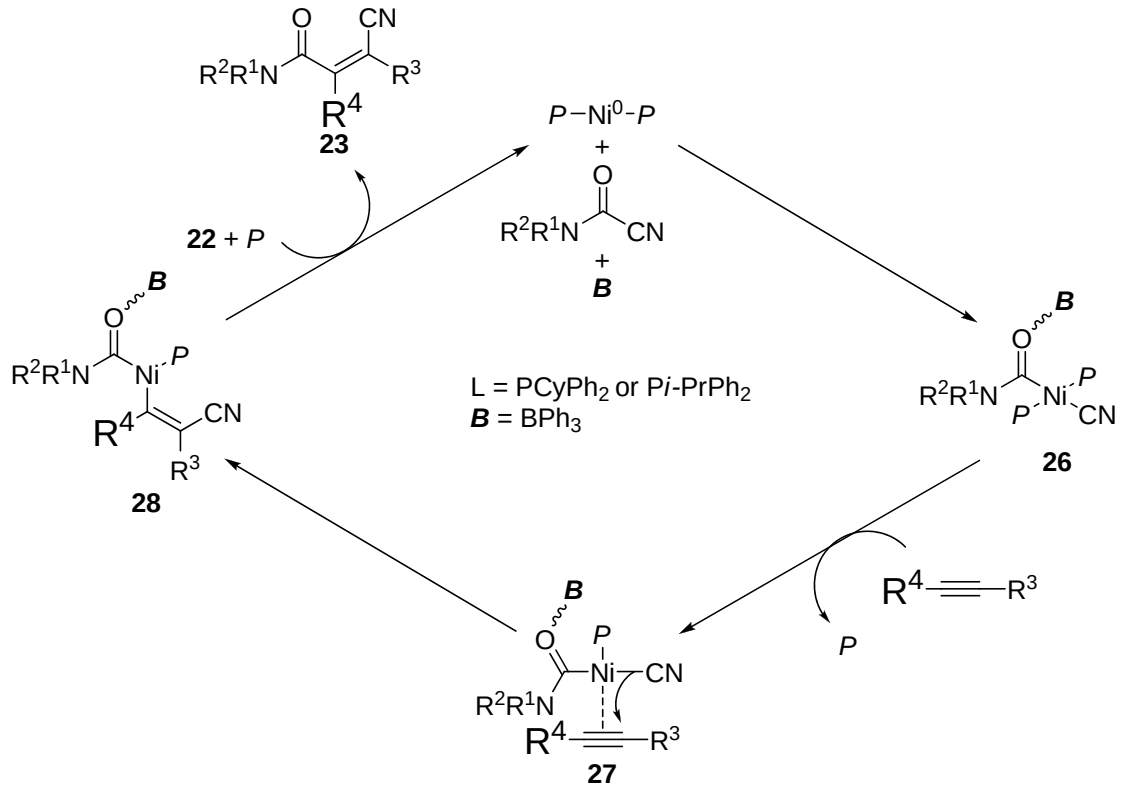
^{13}C NMR

δ_{CN}: 154.8 ppm (t, J_{C-P} = 23.1 Hz)

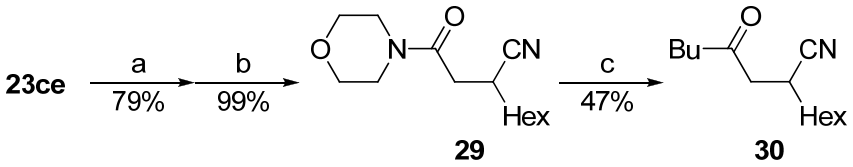
Figure 2. Chemical shifts in ^{13}C NMR of cyanonickel(II) complexes.

Based on these results, the cyanocarbamoylation reaction can be understood by initiation that the C–CN bond in carbamoyl cyanides, oxidatively add to nickel(0) to give oxidative adduct **26** (Scheme 6). The phosphine ligand is then substituted by an alkyne, which then undergoes migratory insertion into the Ni–CN bond at the less hindered carbon of the alkyne to give alkenylnickel intermediate **28**.[26] Insertion of alkynes into Ni–CN bonds energetically possible based on theoretical caluculation.[27] The aminocarbonyl group coordinating to BPh_3 is likely reluctant to undergo the migration. Finally, reductive elimination gives cyanocarbamoylation product **23** and regenerate nickel(0).

Cyanocarbamoylation product **23ce** was transformed to β-cyano ketone **30** by a sequence of protodesilylation, reduction of the double bond, and nucleophilic substitution reaction of the morpholinamide group with an organolithium reagent (Scheme 7).[28]



Scheme 6. Plausible mechanism of cyanocarbamoylation of alkynes.



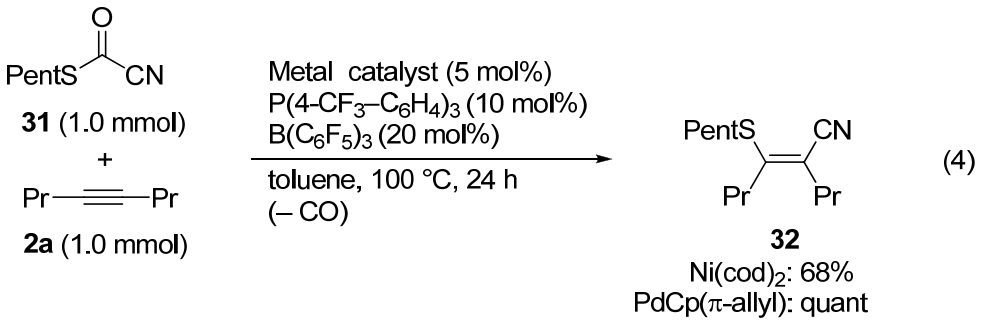
Reagents and Conditions: (a) TBAF, CF_3CO_2H, THF, 0 °C, 5 h; (b) H_2, Pd/C (10 mol%), dioxane, rt, 5 h; (c) BuLi, THF, –78 °C, 30 min.

Scheme 7. Transformations of the cyanocarbamoylation product.

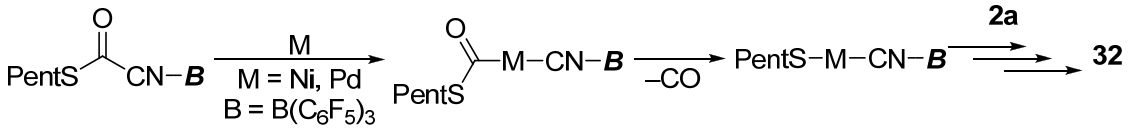
Palladium/B(C_6F_5)$_3$-catalyzed decarbonylative thiocyanation of 4-octyne

The author extended the addition reaction to pentyl thiocyanoformate (**31**) and attempted the reaction with 4-octyne (**2a**) in the presence of $Ni(cod)_2$ (5 mol%), P(4-CF_3–C_6H_4)$_3$ (10 mol%), and B(C_6F_5)$_3$ (15 mol%) in toluene at 100 °C to obtain *cis*-thiocyanation product **32** in 68% yield after 24 h (eq. 4). None of the expected cyanothioesterification product was formed. The regiochemistry of **32** was confirmed by nOe experiments of ^{1}H NMR after the reduction of the cyano group to formyl. Use of a palladium catalyst instead of nickel improved the yield significantly, whereas the absence of Lewis acid cocatalyst, retarded the reaction with both palladium and nickel

catalysts. Although palladium-catalyzed thiocyanation of terminal alkynes has already been reported by Ogawa and coworkers,[29] this reaction represents the first example of thiocyanation of internal alkynes.

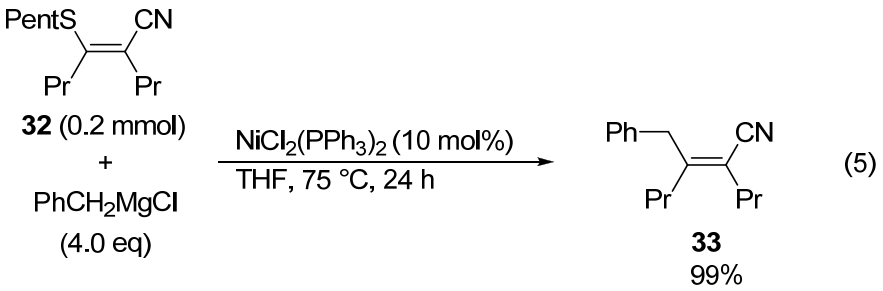


The reaction should be initiated by the oxidative addition of either the C–CN bond or S–CN bond to nickel(0) or palladium(0) followed by decarbonylation to give a RS–M–CN intermediate, which reductively eliminates an thiocyanation product after migratory insertion of an alkyne into either the RS–M or M–CN bond (Scheme 8).[30]



Scheme 8. Plausible mechanism for decarbonylative thiocyanation of 4-octyne (**2a**).

The resulting C–S bond of **32** underwent the Kumada-type cross-coupling reaction with benzylmagnesium chloride in the presence of a nickel catalyst to give formal benzylcyanation product **33** in 99% yield (eq. 5).[31]

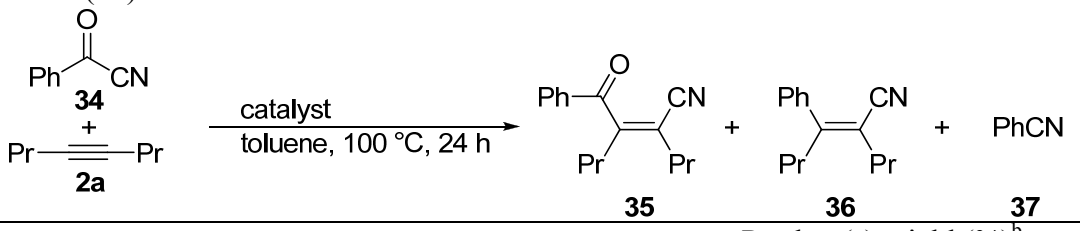


Palladium/BAr$_3$-catalyzed decarbonylative phenylcyanation of 4-octyne

Finally, the author examined benzoylcyanation of 4-octyne (**2a**). In the presence of

a nickel catalyst without Lewis acid, only a small amount of expected *cis*-benzoylcyanation product **35** was obtained (entry 1 of Table 5), along with phenylcyanation product **36** and benzonitrile (**37**). Products **36** and **37** should be derived from decarbonylation of **34**.[32] Whereas addition of a Lewis acid cocatalyst was not effective (entry 2), palladium/BPh_3 catalysts selectively gave **36** (entries 4 and 5). Of ligands examined, $PCyPh_2$ was the best to give **36** in 58% yield after isolation (entry 5). The reaction of benzonitrile (**37**) with 4-octyne (**2a**) under the same conditions gave **36** only in 20% yield, suggesting that insertion of alkynes would take place after the oxidative addition of **34** to palladium(0) followed by decarbonylation.

Table 5. Decarbonylative phenylcyanation of 4-octyne (**2a**) using benzoyl cyanide (**34**).[a]



			Product(s), yield (%)[b]		
Entry	Catalyst (mol%)	Conv. of **34**[b]	**35**	**36**	**37**
1	$Ni(cod)_2$/$2PCy_2Ph$ (5)	38	3	3	15
2	$Ni(cod)_2$/$2PCy_2Ph$/$4BPh_3$ (5)	40	2	3	0
3	PdCp(π-allyl)/$2PCy_2Ph$ (5)	44	0	6	2
4	PdCp(π-allyl)/$2PCy_2Ph$/$4BPh_3$ (5)	75	0	22	0
5	PdCp(π-allyl)/$2PCyPh_2$/$4BPh_3$ (5)	100	0	57 (58)[c]	21

[a] All the reaction was carried out using **34** (0.20 mmol) and **2a** (0.20 mmol) in toluene (0.40 mL). [b] Estimated by GC using tetradecane as an internal standard. [c] Isolated yield obtained with a 1.00 mmol scale reaction.

Conclusion

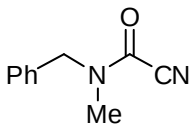
In summary, the author has demonstrated cyanoesterification and cyanocarbamoylation of alkynes proceed with nickel/Lewis acid catalysts. The addition reaction allows stereo- and regioselective preparation of variously functionalized *β*-cyano-substituted acrylates and acrylamides, which are versatile synthetic intermediates for *γ*-aminobutyric acid, *β*-amino acid, *β*-cyano ketone, and 1,2-dicarboxylic acid derivatives. The author also showed that cyanoformate thioesters and cyano ketones react with alkynes under decarbonylation in the presence of nickel or palladium/Lewis acid catalysts.

Experimental

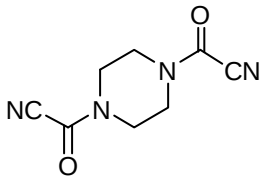
Chemicals.

Anhydrous 1,4-dioxane was purchased from Aldrich and degassed by bubbling an argon gas vigorously for 20 min before use. Carbamoyl cyanides[12b] and thiocyanoformate (**31**)[33,12b] were prepared according to the respective literature procedure.

***N*-Benzyl-*N*-methylcarbamoyl cyanide (22b).** A colorless oil, R_f 0.53 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.20 (m, 5H), 4.77 (s, 1H), 4.60 (s, 1H), 3.18 (s, 1.5H), 2.93 (s, 1.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.0, 144.5, 134.0, 133.6, 129.1, 128.9, 128.7, 128.32, 128.29, 127.5, 110.6, 110.4, 54.7, 50.4, 35.5, 32.3; IR (neat): 3065, 3032, 2934, 2232, 1682, 1497, 1485, 1454, 1427, 1406, 1360, 1292, 1267, 1225, 1115, 1078, 1030, 972, 820, 764, 723, 698, 629, 573, 525 cm^{-1}; HRMS (EI) Calcd for $C_{10}H_{10}N_2O$: M^+, 174.0793. Found: *m*/*z* 174.0792.



1,4-Piperazindicarbonyl dicyanide (22d). A pale yellow solid, mp 221.0–221.5 °C, R_f 0.73 (ethyl acetate). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.88 (s, 2H), 3.74 (s, 4H), 3.60 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 144.1, 111.6, 46.9, 46.3, 42.2, 41.5; IR (KBr): 2996, 2940, 2234, 1678, 1466, 1445, 1435, 1360, 1288, 1238, 1175, 1049, 1017, 974, 922, 719, 704, 627, 534, 550 cm^{-1}. Anal. Calcd for $C_8H_8N_4O_2$; C, 50.00; H, 4.20. Found: C, 49.65; H, 4.14.



Nickel/BAr_3-catalyzed cyanoesterification of alkynes. *A general procedure.*

In a dry box, ethyl cyanoformate (99 mg, 1.00 mmol), an alkyne (1.00 mmol), and tridecane (internal standard, 92 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (13.8 mg, 0.050 mmol), BAr_3 [$B(C_6F_5)_3$: 102 mg, 0.20 mmol; BPh_3: 48 mg, 0.20 mmol], and $P[3,5\text{-}(CF_3)_2\text{–}C_6H_3]_3$ (134 mg, 0.20 mmol) in toluene or dioxane (0.67 mL) placed in a vial. The vial was taken outside the dry box and kept stirred at 35 °C for the time specified in Tables 1 and 2. The resulting mixture was filtered through a silica

gel pad. The filtrate was concentrated *in vacuo*, and the residue was purified by flash column chromatography on silica gel to give the corresponding cyanoesterification products in yields listed in Tables 1 and 2.

Ethyl (*Z*)-3-cyano-2-propylhex-2-enoate (3aa). A pale yellow oil, R_f 0.65 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.32 (q, *J* = 7.1 Hz, 2H), 2.42 (t, *J* = 7.7 Hz, 2H), 2.33 (t, *J* = 7.7 Hz, 2H), 1.67 (sext, *J* = 7.5 Hz, 2H), 1.46 (sext, *J* = 7.5 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.99 (t, *J* = 7.3 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 147.2, 119.2, 117.5, 61.9, 33.4, 31.4, 21.9, 21.4, 14.1, 14.0, 13.7; IR (neat): 2978, 2935, 2872, 2216, 1722, 1816, 1618, 1466, 1460, 1366, 1310, 1300, 1227, 1194, 1130, 1111, 1064, 1030, 848 cm^{-1}; MS (EI) m/z (%) 209 (M^+, 8), 181 (63), 180 (100), 166 (31), 165 (18), 164 (82), 163 (10), 153 (28), 152 (88), 140 (23), 138 (19), 136 (45), 135 (20), 134 (25), 124 (44), 122 (33), 120 (17), 109 (30), 108 (27), 107 (21), 106 (39), 95 (16), 94 (35), 93 (15), 92 (12), 91 (11), 81 (40), 80 (16), 79 (38), 78 (23), 77 (19), 67 (34), 66 (12), 65 (16), 55 (15), 53 (17), 52 (11). Anal. Calcd for $C_{12}H_{19}NO_2$; C, 68.87; H, 9.15. Found: C, 69.14; H, 8.93.

Ethyl (*Z*)-3-cyano-2-(trimethylsilylmethyl)-4-(trimethylsilyl)but-2-enoate (3ab). A pale yellow oil, R_f 0.25 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 1.95 (s, 2H), 1.82 (s, 2H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.17 (s, 9H), 0.07 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 142.1, 119.2, 113.6, 61.8, 25.0, 22.0, 14.1, –0.69, –0.87; IR (neat): 2957, 2901, 2212, 1721, 1715, 1595, 1447, 1414, 1400, 1368, 1306, 1290, 1252, 1213, 1153, 1069, 1020, 939, 851, 797, 758, 698, 637 cm^{-1}. Anal. Calcd for $C_{14}H_{27}NO_2Si_2$; C, 56.51; H, 9.15. Found: C, 56.27; H, 8.89.

Ethyl (*Z*)-3-cyano-2,4-dimethylpent-2-enoate (3ac). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (q, *J* = 7.1 Hz, 2H), 2.90 (sept, *J* = 6.8 Hz, 3H), 2.06 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.19 (d, *J* = 6.6 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 140.4, 126.5, 115.5, 62.0, 29.9, 20.6, 15.4, 14.1; IR (neat): 2974, 2936, 2876, 2212, 1722, 1715, 1614, 1468, 1456, 1393, 1368, 1306, 1283, 1213, 1173, 1128, 1053, 1024, 860, 772, 667 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO_2$; C, 66.27; H, 8.34. Found (as a mixture with **3'ac**): C, 66.51; H, 8.38. The regiochemistry was assigned based on HMBC experiments.

(*Z*)-3-Ethoxycarbonyl-2,4-dimethylpent-2-enenitrile (3'ac). A colorless oil, R_f 0.25 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.32 (q, *J* = 7.1 Hz, 2H), 2.86 (sept, *J* = 6.9 Hz, 3H), 2.00 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.16 (d, *J* = 7.0 Hz, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 154.9, 118.1, 109.2, 61.7, 29.5, 20.2, 16.4, 14.1; IR (neat): 2974, 2938, 2907, 2220, 1728, 1622, 1464, 1389, 1368, 1302, 1209, 1186, 1130, 1030, 839, 814, 758 cm^{-1}.

Ethyl (*Z*)-3-cyano-2,4,4-trimethylpent-2-enoate (3ad). A pale yellow oil, R_f 0.18 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (q, *J* = 7.1 Hz, 2H), 2.20 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.35 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 145.1, 125.7, 116.9, 62.2, 34.9, 30.1, 17.8, 14.0; IR (neat): 2974, 2212, 1728, 1607, 1468, 1370, 1300, 1236, 1150, 1098, 1072, 1044, 858, 777, 669 cm^{-1}. Anal. Calcd for $C_{11}H_{17}NO_2$; C, 67.66; H, 8.78. Found: C, 67.58; H, 8.83. The regiochemistry was assigned based on HMBC experiments.

(*E*)-3-Ethoxycarbonyl-2-(trimethylsilyl)non-2-enenitrile (3ae). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 (q, *J* = 7.1 Hz, 2H), 2.50 (t, *J* = 7.8 Hz, 2H), 1.48–1.22 (m, 8H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 6.9 Hz, 3H), 0.36 (s, 9H); ^{13}C

NMR (101 MHz, $CDCl_3$) δ 165.9, 162.6, 118.2, 117.1, 62.0, 33.8, 31.5, 29.3, 28.5, 22.5, 14.12, 14.07, –0.29; IR (neat): 2959, 2932, 2861, 2214, 1722, 1586, 1466, 1366, 1254, 1202, 1098, 1034, 984, 903, 847, 766, 723, 700, 629 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO_2Si$; C, 64.01; H, 9.67. Found (as a mixure with **3'ae**): C, 64.00; H, 9.41.

Ethyl (*E*)-3-cyano-2-trimethylsilylnon-2-enoate (3'ae). A pale yellow oil, R_f 0.38 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 8.0 Hz, 2H), 1.68–1.56 (m, 2H), 1.42–1.24 (m, 6H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 153.4, 126.9, 116.5, 61.6, 34.0, 31.6, 28.9, 28.3, 22.6, 14.3, 14.1, –0.45; IR (neat): 2959, 2932, 2861, 2216, 1722, 1586, 1464, 1366, 1254, 1242, 1202, 1098, 1034, 982, 847, 766, 725, 700, 629 cm^{-1}. The regiochemistry has been assigned based on structure of **10**.

(*E*)-3-Ethoxycarbonyl-2-methyl-2-trimethylsilylhex-2-enenitrile (3af). A pale yellow oil, R_f 0.23 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.34 (q, *J* = 7.1 Hz, 2H), 2.43 (d, *J* = 7.5 Hz, 2H), 1.86–1.71 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 6H), 0.36 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 162.8, 118.2, 117.0, 62.0, 42.1, 27.9, 22.5, 14.1, –0.04; IR (neat): 2961, 2903, 2874, 2201, 1726, 1578, 1466, 1389, 1368, 1296, 1256, 1225, 1153, 1113, 1096, 1018, 912, 847, 764, 700, 627 cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_2Si$; C, 61.61; H, 9.15. Found (as a mixture with **3'af**): C, 61.66; H, 9.02.

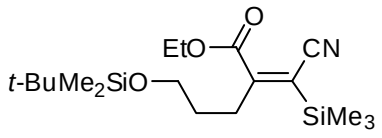
Ethyl (*E*)-3-cyano-5-methyl-2-trimethylsilylhex-2-enoate (3'af). A pale yellow oil, R_f 0.30 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 2.21 (d, *J* = 7.1 Hz, 2H), 2.16–2.01 (m, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.99 (d, *J* = 6.4 Hz, 6H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 154.6, 126.1, 116.5, 61.7, 42.1, 27.7, 22.3, 14.3, –0.27; IR (neat): 2961, 2903, 2874, 2214, 1721, 1584, 1466, 1389, 1370, 1256, 1223, 1190, 1098, 1034, 914, 849, 764, 700, 629 cm^{-1}.

(*E*)-3-Methoxycarbonyl-5-methyl-2-trimethylsilylhex-2-enenitrile (3bf). A pale yellow oil, R_f 028 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 2.43 (d, *J* = 7.3 Hz, 2H), 1.84–1.69 (m, 1H), 0.92 (d, *J* = 6.8 Hz, 6H), 0.36 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 162.6, 118.2, 117.5, 52.5, 42.0, 27.9, 22.4, –0.06; IR (neat): 2959, 2901, 2874, 2201, 1732, 1580, 1466, 1435, 1389, 1370, 1288, 1277, 1256, 1225, 1192, 1153, 1113, 1096, 1034, 974, 905, 893, 847, 764, 700, 627 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2Si$; C, 60.21; H, 8.84. Found: C, 60.29; H, 8.60.

Methyl (*E*)-3-cyano-5-methyl-2-trimethylsilylhex-2-enoate (3'bf). A pale yellow oil, R_f 0.33 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.82 (s, 3H), 2.21 (d, *J* = 7.3 Hz, 2H), 2.16–2.02 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 6H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 154.6, 126.4, 116.5, 52.4, 42.1, 27.7, 22.2, –0.35; IR (neat): 2959, 2901, 2874, 2214, 1726, 1584, 1466, 1433, 1389, 1371, 1256, 1225, 1099, 1026, 951, 920, 907, 849, 764, 700, 629 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2Si$; C, 60.21; H, 8.84. Found: C, 60.00; H, 8.90.

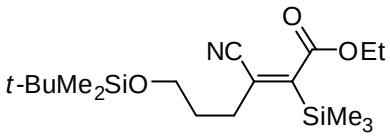
Ethyl (2*E*,6*E*)-3-cyano-7,11-dimethyl-2-trimethylsilyldodeca-2,6,10-trienoate (3'ag). A pale yellow oil, R_f 0.50 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14–5.03 (m, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.40–2.28 (m, 4H), 2.13–1.96 (m, 4H), 1.69 (s, 3H), 1.64 (s, 3H), 1.61 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 153.8, 137.5, 131.4, 126.4, 123.9, 121.1, 116.4, 61.6, 39.7, 34.1, 26.7, 26.6, 25.8, 17.8, 16.3, 14.3, –0.44; IR (neat): 2967, 2918, 2859, 2216, 1722, 1586, 1447, 1385, 1366, 1256, 1211, 1096, 1036, 984, 882, 847, 766, 700, 629 cm^{-1}. Anal. Calcd for $C_{20}H_{33}NO_2Si$; C, 69.11; H, 9.57. Found: C, 69.01; H, 9.68.

(*E*)-6-(*tert*-Butyldimethylsiloxy)-3-ethoxycarbonyl-2-trimethylsilylhex-2-enenitrile



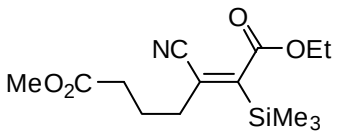
(3ah). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.33 (q, *J* = 7.1 Hz, 2H), 3.65 (t, *J* = 5.8 Hz, 2H), 2.61 (t, *J* = 8.1 Hz, 2H), 1.69–1.59 (m, 2H), 1.38 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.37 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 162.1, 118.3, 117.9, 62.4, 62.0, 31.6, 30.7, 26.0, 18.5, 14.2, –0.34, 5.2; IR (neat): 2957, 2930, 2859, 2201, 1728, 1574, 1472, 1393, 1368, 1302, 1256, 1190, 1144, 1101, 1020, 963, 845, 777, 704, 662, 627 cm^{-1}. Anal. Calcd for $C_{18}H_{35}NO_3Si_2$; C, 58.49; H, 9.54. Found (as a mixture with **3'ah**): C, 58.52; H, 9.41.

Ethyl (*E*)-6-(*tert*-butyldimethylsiloxy)-3-cyano-2-trimethylsilylhex-2-enoate (3'ah).



A pale yellow oil, R_f 0.28 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 3.69 (t, *J* = 5.7 Hz, 2H), 2.45 (t, *J* = 8.1 Hz, 2H), 1.84–1.78 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.28 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 153.8, 126.4, 116.5, 62.0, 61.6, 31.5, 31.0, 26.0, 18.4, 14.3, –0.6, –5.2; IR (neat): 2957, 2930, 2901, 2859, 2216, 1721, 1587, 1472, 1464, 1447, 1410, 1389, 1364, 1256, 1217, 1107, 1053, 1036, 1007, 926, 841, 777, 735, 702, 629 cm^{-1}.

Ethyl 7-methyl (*E*)-3-cyano-2-trimethylsilylhept-2-endioate (3'ai). A pale yellow oil,



R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 3.69 (s, 3H), 2.48–2.32 (m, 4H), 2.02–1.92 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.27 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 169.0, 154.8, 125.4, 116.2, 61.7, 51.8, 33.0, 32.9, 23.4, 14.3, –0.6; IR (neat): 2957, 2905, 2216, 1738, 1721, 1586, 1439, 1368, 1256, 1204, 1142, 1096, 1032, 991, 895, 849, 766, 702, 629 cm^{-1}. Anal. Calcd for $C_{14}H_{23}NO_4Si$; C, 56.54; H, 7.79. Found : C, 56.61; H, 7.56.

(*E*)-3-Ethoxycarbonyl-6-phthalimidoyl-2-trimethylsilylhex-2-enenitrile (3aj). A pale yellow oil, R_f 0.35 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.81 (m, 2H), 7.76–7.69 (m, 2H), 4.31 (q, *J* = 7.0 Hz, 2H), 3.74 (t, *J* = 7.0 Hz, 2H), 2.58 (t, *J* = 8.2 Hz, 2H), 1.89–1.78 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 0.34 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 165.2, 160.2, 134.0, 131.8, 123.2, 119.2, 118.0, 62.2, 37.5, 31.2, 27.6, 14.1, –0.4; IR (neat): 3470, 3061, 2959, 2938, 2857, 2224, 2201, 1771, 1728, 1722, 1713, 1614, 1582, 1470, 1435, 1395, 1371, 1256, 1229, 1188, 1152, 1105, 1017, 885, 849, 797, 764, 721, 627, 530 cm^{-1}. Anal. Calcd for $C_{20}H_{24}N_2O_4Si$; C, 62.47; H, 6.29. Found (as a mixture with **3'aj**): C, 62.36; H, 6.16.

Ethyl (*E*)-3-cyano-6-phthalimidoyl-2-trimethylsilylhex-2-enoate (3'aj). A pale yellow oil, R_f 0.35 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.82 (m, 2H), 7.76–7.70 (m, 2H), 4.26 (q, *J* = 7.0 Hz, 2H), 3.78 (t, *J* = 6.8 Hz, 2H), 2.41 (t, *J* = 8.4 Hz, 2H), 2.08–1.96 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 0.23 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 167.9, 154.5, 134.0, 131.8, 125.1, 123.2, 116.0, 61.7, 37.2, 31.5, 27.6, 14.2, –0.6; IR (neat): 2959, 2903, 2216, 1771, 1728, 1715, 1722, 1699, 1682, 1614, 1586, 1470, 1454, 1441, 1435, 1393, 1371, 1360, 1337, 1300, 1254, 1215, 1190, 1107, 1030, 905, 847, 795, 766, 719, 629, 530 cm^{-1}.

Desilylation of 3'ae. To a solution of **3'ae** (0.63 g, 2.2 mmol) in THF (66 mL) were added CF_3CO_2H (0.67 g, 5.9 mmol) and a 1.0 M solution of TBAF (8.8 mL, 8.8 mmol) in THF successively at 0 °C. The resulting reaction mixture was stirred at 0 °C for 1.5 h, before quenching with water. The organic layer was separated, and the aqueous layer was extracted with hexane. The combined organic layers were washed with water, saturated $NaHCO_3$ aqueous solution, and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 12 : 1 as an eluent) to give ethyl

(*Z*)-3-cyanonon-2-enoate (0.40 g, 88%) and its stereoisomer ethyl (*E*)-3-cyanonon-2-enoate (20 mg, 5%).

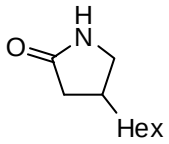
Ethyl (*Z*)-3-cyanonon-2-enoate. A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.30 (t, *J* = 1.5 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.39 (td, *J* = 7.6, 1.5 Hz, 2H), 1.64 (quint, *J* = 7.5 Hz, 2H), 1.42–1.22 (m, 6H), 1.34 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 132.0, 128.0, 115.9, 61.6, 36.0, 31.4, 28.4, 27.5, 22.5, 14.2, 14.1; IR (neat): 2957, 2932, 2861, 2222, 1728, 1638, 1466, 1371, 1348, 1281, 1221, 1142, 1099, 1034, 891, 725, 656 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO_2$; C, 68.87; H, 9.15. Found: C, 68.62; H, 8.96. The regiochemistry has been assigned based on structure of **10**.

Ethyl (*E*)-3-cyanonon-2-enoate. A pale yellow oil, R_f 0.28 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (d, *J* = 0.7 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.78 (t, *J* = 7.7 Hz, 2H), 1.63 (quint, *J* = 7.6 Hz, 2H), 1.44–1.20 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 132.1, 131.4, 118.2, 61.3, 31.5, 30.1, 28.7, 28.0, 22.6, 14.2, 14.1; IR (neat): 2959, 2932, 2861, 2220, 1728, 1630, 1468, 1371, 1350, 1281, 1561, 1219, 1184, 1150, 1096, 1032, 889, 725, 638 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO_2$; C, 68.87; H, 9.15. Found: C, 68.63; H, 9.06

Hydrogenation of Ethyl (*Z*)-3-cyanonon-2-enoate. To a suspension of Pd on carbon (10 wt%, 21 mg, 0.020 mmol) in dioxane (1.00 mL) was added ethyl (*Z*)-3-cyanonon-2-enoate (42 mg, 0.20 mmol) at room temterature, and the resulting mixture was vigorously stirred at room temperature for 1.5 h under a hydrogen atmosphere (1 atm) before dilution with diethyl ether. Filtration through a Celite pad and concentration *in vacuo* gave ethyl 3-cyanononanoate (**9**, 41 mg, 97%) as a colorless oil, R_f 0.20 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (q, *J* = 7.1 Hz, 2H), 3.02 (quint, *J* = 7.1 Hz, 1H), 2.70 (dd, *J* = 16.5, 7.5 Hz, 1H), 2.55 (dd, *J* = 16.5, 6.8 Hz, 1H), 1.70–1.22

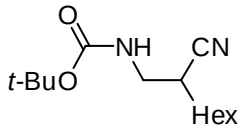
(m, 10H), 1.29 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 121.0, 61.3, 36.9, 31.9, 31.5, 28.7, 27.7, 27.0, 22.6, 14.3, 14.1; IR (neat): 2957, 2930, 2859, 2241, 1738, 1694, 1468, 1422, 1375, 1352, 1252, 1192, 1113, 1098, 1030, 862, 725 cm^{-1}; HRMS (FAB+) Calcd for $C_{12}H_{22}NO_2$: $[M+H]^+$, 212.1651. Found: m/z 212.1649.

γ-Lactam synthesis from 9. Sodium borohydride (73 mg, 1.94 mmol) was added portionwise to a solution of **9** (41 mg, 0.194 mmol) and $CoCl_2$ (50 mg, 0.39 mmol) in EtOH (5.4 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 h and then at room temperature for 11 h. The reaction was quenched with a 1 M HCl aqueous solution, and the resulting mixture was stirred at room temperature for 0.5 h. After neutralization with a saturated $NaHCO_3$ aqueous solution, the mixture was extracted with diethyl ether. Combined organic layers were washed three times with water and then with brine and dried over anhydrous $MgSO_4$. The residue was purified by flash column chromatography on silica gel to give 4-hexylpyrrolidin-2-one (**10**, 23 mg, 71%)[34] as a colorless oil, R_f 0.05 (hexane–ethyl acetate = 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (br s, 1H), 3.48 (dd, J = 9.4, 6.9 Hz, 1H), 3.00 (dd, J = 9.4, 6.7 Hz, 1H), 2.51–2.37 (m, 2H), 1.99 (dd, J = 19.9, 11.5 Hz, 1H), 1.45 (q, J = 6.7 Hz, 2H), 1.28 (br s, 8H), 0.88 (t, J = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.3, 48.1, 36.9, 35.0, 34.7, 31.8, 29.3, 27.5, 22.7, 14.2; IR (neat) 3235, 2955, 2926, 2855, 1703, 1694, 1682, 1489, 1462, 1456, 1425, 1377, 1281, 1069, 725, 696 cm^{-1}. Anal. Calcd for $C_{10}H_{19}NO$; C, 70.96; H, 11.31. Found: C, 71.03; H, 11.19.



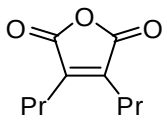
Synthesis of Boc-protected β-cyano amide 11. $Ba(OH)_2$ (123 mg, 0.40 mmol) was added to a solution of crude **9** in MeOH (2.0 mL) at room temperature, and the resulting mixture was stirred at the same temperature for 4 h before quenching with a 1 M HCl aqueous solution. The resulting mixture was extracted with dichloromethane. The combined organic layers were washed with 1 M HCl aq. and then with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue and Et_3N (61 mg, 0.60 mmol) were dissolved in *t*-BuOH (0.25 mL), and to this solution was added diphenylphospholyl azide (73 mg, 0.30 mmol) at room temperature. The resulting

mixture was stirred at 75 °C for 11 h. The reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography on silica gel to give



tert-butyl *N*-2-cyanooctylcarbamate (**11**, 20 mg, 40%) as a colorless oil, R_f 0.18 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.95 (br s, 1H), 3.52–3.36 (m, 1H), 3.26–3.10 (m, 1H), 2.92–2.86 (m, 1H), 1.66–1.18 (m, 10H), 1.45 (s, 9H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.5, 121.0, 80.1, 42.4, 33.3, 31.5, 29.6, 28.8, 28.4, 27.0, 22.6, 14.1; IR (KBr) 3358, 2957, 2930, 2861, 2241, 1713, 1697, 1589, 1520, 1456, 1393, 1368, 1275, 1254, 1171, 1072, 1026, 1011, 966, 864, 781, 725, 689 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{26}N_2O_2$: M^+, 254.1994. Found: *m*/*z* 254.1985.

Synthesis of maleic anhydride 12. To a solution of NaOH (18 mg, 0.45 mmol) in EtOH/H_2O (0.30 mL, 2 : 1) was added **3aa** (21 mg, 0.100 mmol) at room temperature, and the resulting mixture was stirred at 80 °C for 4 h before quenching with a 1 M HCl aqueous solution. The resulting mixture was extracted with dichloromethane. The combined organic layers were washed with successively 1 M HCl, a saturated $NaHCO_3$ aqueous solution and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give 2,3-dipropylbutenedioic anhydride (**12**, 10.5 mg, 65%) as a colorless oil, R_f 0.13



(hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (t, J = 7.7 Hz, 4H), 1.63 (sext, J = 7.5 Hz, 4H), 0.99 (t, J = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 144.3, 26.4, 21.5, 14.1; IR (neat) 2967, 2936, 2876, 1846, 1767, 1665, 1466, 1383, 1275, 1225, 1134, 1090, 953, 916, 746 cm^{-1}. Anal. Calcd for $C_{10}H_{14}O_3$; C, 65.91; H, 7.74. Found: C, 66.19; H, 7.65.

Desilylation of 3'bf. To a solution of **3'bf** (0.60 g, 2.5 mmol) in THF (75 mL) were added CF_3CO_2H (0.78 g, 6.8 mmol) and a 1.0 M solution of TBAF (10.0 mL, 10.0 mmol) in THF successively at 0 °C. The resulting reaction mixture was stirred at 0 °C for 2 h before quenching with water. The organic layer was separated, and the aqueous layer was extracted with hexane. The combined organic layers were washed successively with water, saturated $NaHCO_3$ aqueous solution, and brine, dried over

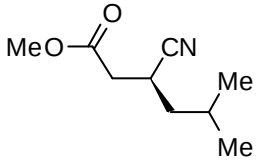
anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 12 : 1 as an eluent) to give methyl (*Z*)-3-cyano-5-methylhex-2-enoate (**13**, 380 mg, 90%) and its stereoisomer methyl (*E*)-3-cyano-5-methylhex-2-enoate (*trans*-**13**, 30 mg, 6%).

Methyl (*Z*)-3-cyano-5-methylhex-2-enoate (13). A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (t, *J* = 1.3 Hz, 1H), 3.83 (s, 3H), 2.27 (dd, *J* = 7.2, 1.2 Hz, 2H), 2.14–1.99 (m, 1H), 0.97 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 132.5, 127.4, 115.9, 52.3, 44.9, 27.2, 22.0; IR (neat): 2961, 2874, 2222, 1732, 1634, 1468, 1435, 1389, 1362, 1339, 1288, 1238, 1215, 1169, 1146, 1101, 1013, 893, 818, 777, 752, 660, 586 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_2$; C, 64.65; H, 7.84. Found: C, 64.95; H, 7.90.

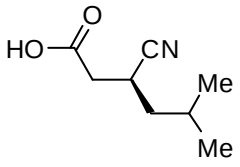
Methyl (*E*)-3-cyano-5-methylhex-2-enoate (*trans*-13). A pale yellow oil, R_f 0.20 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (t, *J* = 1.2 Hz, 1H), 3.78 (s, 3H), 2.69 (dd, *J* = 7.3, 1.1 Hz, 2H), 2.11–1.95 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 132.3, 130.9, 118.2, 52.1, 38.5, 28.1, 22.1; IR (neat): 2961, 2874, 2222, 1732, 1636, 1468, 1435, 1362, 1339, 1288, 1238, 1215, 1146, 1101, 1013, 893, 818, 777, 752, 662, 586 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_2$; C, 64.65; H, 7.84. Found: C, 64.92; H, 7.95.

Asymmetric conjugated reduction of 13 catalyzed by a chiral Cu/(*R*)-binap catalyst.[24] To a solution of CuCl (1.00 mg, 10.0 μmol), NaO*t*-Bu (1.00 mg, 10.0 μmol) and (*R*)-binap (6.2 mg, 10.0 μmol) in toluene (0.40 mL) were added sequentially polymethylhydrosiloxane (PMHS, 30 mg, 0.40 mmol), *t*-BuOH (17.8 mg, 0.24 mmol), and **13** (33 mg, 0.20 mmol). The resulting mixture was stirred at room temperature for 24 h before dilution with dichloromethane and quenching with MeOH. The resulting mixture was extracted with dichloromethane. The combined organic layers were washed with a saturated NH_4Cl aqueous solution and brine, dried over anhydrous $MgSO_4$,

concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give methyl (*S*)-3-cyano-5-methyl-hexanoate (**14**, 32 mg, 94%) of 80% ee as a colorless oil, R_f 0.13 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.13–3.01 (m, 1H), 2.71 (dd, *J* = 16.7, 7.5 Hz, 1H), 2.56 (dd, *J* = 16.7, 6.7 Hz, 1H), 1.94–1.80 (m, 1H), 1.70–1.60 (m, 1H), 1.40–1.28 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 121.0, 52.3, 40.9, 37.0, 26.2, 25.9, 23.0, 21.3; IR (neat): 2959, 2872, 2241, 1742, 1686, 1468, 1458, 1439, 1370, 1261, 1213, 1175, 1115, 1017, 991, 889, 806 cm^{-1}; HRMS (FAB+) Calcd for $C_9H_{16}NO_2$: $[M+H]^+$, 170.1181. Found: *m*/*z* 170.1179. The ee was estimated by chiral GC analysis of an ethereal solution of **14** with a Chirasil-DEX CB column, isothermal 80 °C for 60 min and then elevated temperature to 150 °C in 70 min. Retention times: 83.4 min [(*R*)-enatiomer], 83.9 min [(*S*)-enatiomer]. $[\alpha]^{28}_D$ –10.4 (*c* 0.50, $CHCl_3$).



Hydrolysis of 14.[22a] Barium hydroxide (81 mg, 0.26 mmol) was added to **14** (23 mg, 0.132 mmol) in methanol (1.30 mL) at room temperature. The resulting mixture was stirred at the same temperature for 4 h. The reaction was quenched with a 1 M HCl aqueous solution and the resulting mixture was extracted with dichloromethane. The combined organic layers were washed with 1 M HCl aq. and brine, dried over anhydrous Na_2SO_4, concentrated *in vacuo* to give methyl (*S*)-3-cyano-5-methylhexanoate (**15**, 21 mg, quantitative yield) as a colorless oil, R_f 0.13 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (br s, 1H), 3.12–2.98 (m, 1H), 2.78 (dd, *J* = 17.0, 7.7 Hz, 1H), 2.63 (dd, *J* = 17.0, 6.4 Hz, 1H), 1.96–1.80 (m, 1H), 1.74–1.60 (m, 1H), 1.42–1.32 (m, 1H), 0.98 (t, *J* = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 120.7, 40.7, 36.9, 26.2, 25.7, 23.0, 21.3; IR (neat): 3183, 2961, 2932, 2874, 2243, 1738, 1722, 1715, 1470, 1416, 1391, 1371, 1269, 1223, 1175, 1113, 924, 893, 816, 758, 667, 619 cm^{-1}; $[\alpha]^{28}_D$ –12.0 (*c* 0.50, $CHCl_3$).



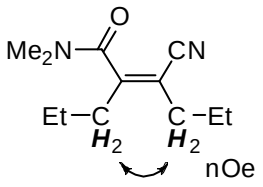
Synthesis of 13 by nickel-catalyzed three component cyanoesterificaction of 18. In a dry box, methyl chloroformate (**16**, 104 mg, 1.10 mmol), trimethylsilyl cyanide (**17**, 109

mg, 1.10 mmol) and **18** (82 mg, 1.00 mmol) were placed in a vial. To this was added a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and $P(2\text{-furyl})_3$ (23 mg, 0.20 mmol) in toluene (0.40 mL). The vial was taken outside the dry box and heated at 100 °C for 24 h. The resulting reaction mixture was filtered through a silica gel pad and concentrated *in vacuo*. Purification of the residue by flash silica gel column chromatography gave methyl (*Z*)-3-cyano-5-methylhex-2-enoate (**13**, 37 mg, 22%) and its stereoisomer methyl (*E*)-3-cyano-5-methylhex-2-enoate (*trans*-**13**, 8.5 mg, 5%).

Nickel/BPh_3-catalyzed carbamoylcyanation of alkynes. *A general procedure.*

In a dry box, a carbamoyl cyanide (1.00 mmol), an alkyne (1.00 mmol), and tetradecane (internal standard, 99 mg, 0.50 mmol) were added sequentially to a solution of $Ni(cod)_2$ (13.8 mg, 0.050 mmol), BPh_3 (36 mg, 0.150 mmol), and $PRPh_2$ ($PCyPh_2$: 27 mg, 0.100 mmol; P*i*-$PrPh_2$: 23 mg, 0.100 mmol) in toluene or dioxane (2.0 mL) placed in a vial. The vial was closed, taken outside the dry box, and heated at 80 °C for the time and specified in Tables 3 and 4. The resulting mixture was filtered through a silica gel pad and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give the corresponding cyanoesterification products in yields listed in Tables 3 and 4.

(*Z*)-3-Cyano-*N*,*N*-dimethyl-2-propylhex-2-enamide (23aa). A pale yellow oil, R_f 0.25 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (s, 6H), 2.38 (br t, *J* = 7.6 Hz, 2H), 2.26 (t, *J* = 7.6 Hz, 2H), 1.64 (sext, *J* = 7.4 Hz, 2H), 1.49 (sext, *J* = 7.6 Hz, 2H), 0.99 (t, *J* = 7.1 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 153.0, 117.4, 111.8, 37.7, 34.6, 32.9, 31.2, 21.4, 21.0, 14.3, 13.7; IR (neat): 2965, 2934, 2874, 2212, 1643, 1634, 1505, 1456, 1398, 1341, 1279, 1258, 1169, 1111, 1087, 1059, 1020, 741, 704 cm^{-1}; MS (EI) *m/z* (%) 208 (M^+, 88), 207 (M^+–1, 19), 194 (18), 193 (88), 180 (59), 179 (100), 177 (11), 168 (11), 166 (12), 165 (75), 164 (89), 163 (35), 154 (35), 152 (12), 151 (53), 148 (13), 140 (13), 138 (14), 137 (49), 136 (25), 135 (24), 134 (20), 123 (16), 122 (17), 121 (14), 120 (17), 109 (23), 108 (15), 107 (18), 106 (25), 95 (17), 94 (57), 93 (15), 92 (11), 91 (13), 81 (20), 80 (14), 79 (24), 78 (20), 77 (17), 72



(93), 67 (41), 66 (11), 65 (13), 55 (20), 53 (12). Anal. Calcd for $C_{12}H_{20}N_2O$; C, 69.19; H, 9.68. Found: C, 69.42; H, 9.41.

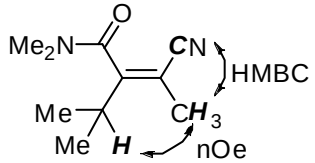
(*Z*)-*N*-Benzyl-3-cyano-2propyl-*N*-methylhex-2-enamide (23ba). A pale yellow oil, R_f 0.43 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.20 (m, 3H), 7.22 (d, *J* = 7.0 Hz, 2H), 4.69 (s, 1.4H), 4.55 (s, 0.6H), 2.92 (s, 0.9H), 2.91 (s, 2.1H), 2.42 (br, 2H), 2.31–2.23 (m, 2H), 1.70–1.46 (m, 4H), 1.04–0.94 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 168.6, 153.1, 152.7, 136.0, 135.3, 128.8, 128.5, 128.3, 127.8, 127.5, 127.1, 117.6, 117.4, 112.8, 111.9, 54.1, 50.3, 34.9, 33.1, 33.0, 32.3, 31.31, 31.27, 21.5, 21.4, 21.0, 14.4, 14.3, 13.7; IR (neat): 2965, 2932, 2874, 2212, 1640, 1634, 1495, 1454, 1404, 1381, 1358, 1312, 1290, 1256, 1101, 1059, 1028, 947, 916, 733, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{24}N_2O$; C, 76.02; H, 8.51. Found: C, 76.00; H, 8.40.

***N*-[(*Z*)-3-cyano-2-propylhex-2-enoyl]morpholine (23ca).** A pale yellow oil, R_f 0.23 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74 (br, 6H), 3.47 (br, 2H), 2.37 (br, 2H), 2.27 (t, *J* = 7.6 Hz, 2H), 1.60 (sext, *J* = 7.5 Hz, 2H), 1.48 (br sext, *J* = 7.4 Hz, 2H), 0.992 (t, *J* = 7.1 Hz, 3H), 0.988 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 152.1, 117.4, 112.3, 66.6, 66.5, 46.9, 42.0, 32.9, 31.3, 21.4, 21.1, 14.3, 13.7; IR (neat): 2965, 2932, 2872, 2212, 1643, 1634, 1462, 1435, 1381, 1362, 1302, 1288, 1269, 1236, 1207, 1115, 1069, 1036, 1108, 957, 928, 891, 847, 743, 588, 573 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{22}N_2O_2$: M^+, 250.1681. Found: *m*/*z* 250.1683.

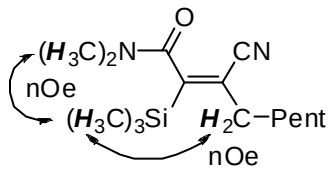
1,4-Bis[(*Z*)-3-cyano-2-propylhex-2-enoyl]piperazin (23da). A colorless solid, mp 143.6–144.2 °C, R_f 0.15 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.50–3.10 (br m, 8H), 2.70–2.16 (br m, 4H), 2.27 (q, *J* = 7.6 Hz, 4H), 1.64 (sext, *J* = 7.4 Hz, 4H), 1.47 (q, *J* = 7.0 Hz, 4H), 0.99 (t, *J* = 6.8 Hz, 6H), 0.98 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 167.0, 152.4, 117.5, 112.6, 46.5, 46.0, 41.4, 41.0, 33.0, 32.9, 31.2, 21.4, 21.2, 21.1, 14.3, 13.7, 13.6;

IR (KBr): 2959, 2932, 2872, 2207, 1640, 1618, 1464, 1437, 1387, 1364, 1352, 1296, 1290, 1279, 1200, 1179, 1113, 1086, 1071, 1051, 1028, 1007, 982, 941, 789, 762, 669, 625, 592, 552, 525, 449 cm^{-1}. Anal. Calcd for $C_{24}H_{36}N_4O_2$; C, 69.87; H, 8.80. Found: C, 69.57; H, 8.65. Colorless single crystals were obtained by recrystalization from hexane and dichloromethane suitable for X-ray crystallographic analysis.

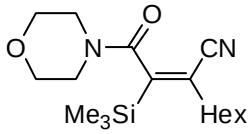
(*Z*)-3-Cyano-*N*,*N*-dimethyl-2-isopropylbut-2-enamide (23ad). A pale yellow oil, R_f 0.13 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.04 (s, 6H), 2.87 (sept, J = 6.9 Hz, 1H), 1.97 (s, 3H), 1.25 (d, J = 7.0 Hz, 3H), 1.06 (d, J = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 158.3, 118.2, 105.4, 37.8, 34.3, 30.2, 22.1, 19.2, 15.5; IR (neat): 2969, 2934, 2876, 2216, 1643, 1634, 1504, 1468, 1462, 1454, 1402, 1366, 1277, 1161, 1121, 1053, 1007, 860, 746, 712, 667, 552 cm^{-1}. Anal. Calcd for $C_{10}H_{16}N_2O$; C, 66.63; H, 8.95. Found: C, 67.03; H, 9.06. The regiochemical assignment was made based on HMBC experiment.



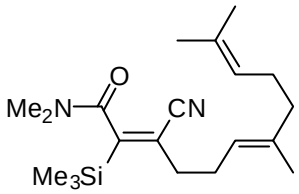
(*E*)-3-Cyano-*N*,*N*-dimethyl-2-(trimethylsilyl)non-2-enamide (23ae). A pale yellow oil, R_f 0.25 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (s, 3H), 2.98 (s, 3H), 2.31 (t, J = 7.9 Hz, 2H), 1.74–1.51 (m, 2H), 1.45–1.22 (m, 6H), 0.90 (t, J = 6.2 Hz, 3H), 0.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 157.4, 123.5, 116.7, 37.6, 34.4, 33.8, 31.6, 29.0, 28.3, 22.6, 14.1, –0.54; IR (neat): 2957, 2930, 2861, 2211, 1634, 1584, 1493, 1462, 1393, 1267, 1254, 1161, 1098, 1057, 1001, 901, 878, 847, 764, 702, 625 cm^{-1}; Anal. Calcd for $C_{15}H_{28}N_2OSi$; C, 64.23; H, 10.06. Found: C, 64.17; H, 9.81. The regiochemical assignment was also supported by ^1H NMR nOe experiments of (*Z*)-3-cyano-*N*,*N*-dimethylnon-2-enamide (*vide infra*).



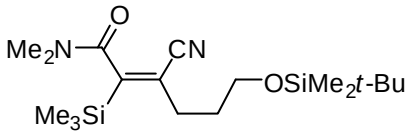
***N*-[(*E*)-3-Cyano-2-trimethylsilylnon-2-enoyl]morpholine (23ce).** A yellow oil, R_f 0.28 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.88–3.44 (m, 7H), 3.36–3.26 (m, 1H), 2.32 (t, J = 7.9 Hz, 2H), 1.70–1.52 (m, 2H), 1.44–1.24 (m, 6H), 0.90 (t, J = 6.7 Hz, 3H),



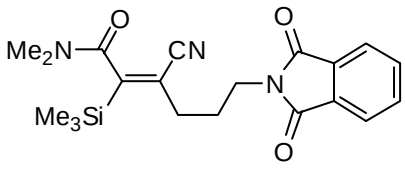
0.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 156.4, 124.3, 116.6, 66.62, 66.55, 46.8, 41.6, 33.8, 31.5, 29.0, 28.3, 22.6, 14.1, –0.48; IR (neat): 2957, 2930, 2859, 2211, 1634, 1456, 1435, 1362, 1300, 1275, 1250, 1117, 1067, 986, 849, 764, 704, 629, 579 cm^{-1}. Anal. Calcd for $C_{17}H_{30}N_2O_2Si$; C, 63.31; H, 9.38. Found: C, 63.59; H, 9.24.

(2*E*,6*E*)-3-Cyano-*N*,*N*,7,11-tetramethyl-2-(trimethylsilyl)dodeca-2,7,11-trienamide (23ag). 

A yellow oil, R_f 0.33 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15–5.03 (m, 2H), 3.03 (s, 3H), 2.98 (s, 3H), 2.40–2.30 (m, 4H), 2.12–1.95 (m, 4H), 1.68 (s, 3H), 1.65 (s, 3H), 1.60 (s, 3H), 0.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 157.9, 137.4, 131.4, 123.9, 123.2, 121.2, 116.6, 39.8, 37.5, 34.4, 33.9, 26.65, 26.62, 25.8, 17.8, 16.3, –0.51; IR (neat): 2965, 2922, 2857, 2211, 1634, 1584, 1497, 1454, 1395, 1265, 1254, 1163, 1109, 1057, 999, 887, 845, 764, 702, 625, 548 cm^{-1}. Anal. Calcd for $C_{20}H_{34}N_2OSi$; C, 69.31; H, 9.89. Found: C, 69.07; H, 9.63.

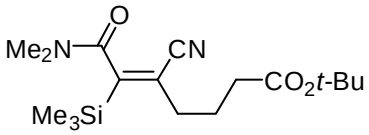
(*E*)-3-Cyano-6-(*tert*-butyldimethylsiloxy)-*N*,*N*-dimethyl-2-(trimethylsilyl)hex-2-enamide (23ah). 

A yellow oil, R_f 0.25 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (t, *J* = 5.7 Hz, 2H), 3.03 (s, 3H), 2.98 (s, 3H), 2.51–2.37 (m, 2H), 1.91–1.72 (m, 2H), 0.90 (s, 9H), 0.27 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 157.9, 123.0, 116.7, 62.0, 37.6, 34.4, 31.5, 30.7, 26.0, 18.4, –0.64, –0.52; IR (neat): 2955, 2930, 2897, 2859, 2212, 1643, 1634, 1586, 1495, 1472, 1462, 1454, 1393, 1362, 1254, 1165, 1103, 1005, 964, 887, 841, 777, 702, 634, 625 cm^{-1}. Anal. Calcd for $C_{18}H_{36}N_2O_2Si_2$; C, 58.64; H, 9.84. Found: C, 58.35; H, 9.56.

(*E*)-3-Cyano-*N*,*N*-dimethyl-6-phthalimidoyl-2-(trimethylsilyl)hex-2-enamide (23aj). 

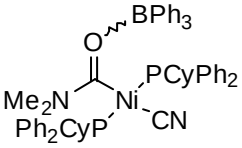
A pale yellow solid, mp 92.7–93.3 °C, R_f 0.20 (hexane–ethyl acetate = 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91–7.80 (m, 2H), 7.79–7.70 (m, 2H), 3.78 (td, *J* = 6.9, 3.4 Hz, 2H), 3.02 (s, 3H), 2.97 (s, 3H), 2.40 (t, *J* = 8.3 Hz, 2H), 2.12–1.90 (m, 2H), 0.22 (s, 9H); ^{13}C NMR (101 MHz,

$CDCl_3$) δ 169.5, 167.9, 158.7, 134.0, 131.7, 123.2, 121.7, 116.3, 37.6, 37.2, 34.5, 31.2, 27.7, –0.69; IR (neat): 2959, 2214, 1770, 1713, 1630, 1584, 1497, 1464, 1456, 1437, 1398, 1377, 1339, 1260, 1252, 1207, 1188, 1169, 1107, 1086, 1053, 1038, 1030, 1003, 903, 880, 845, 793, 762, 719, 623, 530 cm^{-1}. Anal. Calcd for $C_{20}H_{25}N_3O_3Si$; C, 62.63; H, 6.57. Found: C, 62.50; H, 6.60.

(*E*)-6-(*tert*-Butoxycarbonyl)-3-cyano-*N*,*N*-dimethyl-2-(trimethylsilyl)hex-2-enamide (23ak). 

A yellow oil, R_f 0.20 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 3.03 (s, 3H), 2.98 (s, 3H), 2.40–2.34 (m, 2H), 2.31 (td, J = 7.1, 1.8 Hz, 2H), 2.00–1.81 (m, 2H), 1.45 (s, 9H), 0.26 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 169.7, 158.5, 122.4, 116.4, 80.7, 37.6, 34.6, 34.4, 32.8, 28.2, 23.6, –0.60; IR (neat): 2974, 2934, 2212, 1728, 1634, 1497, 1456, 1395, 1368, 1256, 1157, 1057, 1001, 897, 887, 847, 756, 702, 625 cm^{-1}; HRMS (EI) Calcd for $C_{17}H_{30}N_2O_3Si$: M^+, 338.2026. Found: *m*/*z* 338.2029.

Sythesis of *trans*-(Ph_2CyP)Ni(CN)(CO(BPh_3)NMe_2) (24). In a dry box, a benzene solution (3.5 mL) of $Ni(cod)_2$ (138 mg, 0.50 mmol) and $PCyPh_2$ (0.27 g, 1.00 mmol) was added to **22a** (49 mg, 0.50 mmol) and BPh_3 (121 mg, 0.50 mmol) at room temperature. The resulting dark red solution was concentrated *in vacuo* to give precipitates, which was washed with hexane to give *trans*-(Ph_2CyP)Ni(CN)(CO(BPh_3)NMe_2) (**24**, 0.38 g, 80%) as a pale yellow powder, ^1H NMR (400 MHz, C_6D_6) δ 7.60–7.52 (m, 6H), 7.50–7.40 (m, 6H), 7.38–7.30 (m, 6H), 7.28–7.20 (m, 12H), 7.10–6.92 (m, 15H), 2.72 (s, 3H), 2.55 (br t, J = 11.9 Hz, 2H), 2.24–1.96 (m, 4H), 2.17 (s, 3H), 1.54–0.60 (m, 16H); ^{13}C NMR (101 MHz, C_6D_6) δ 193.4 (t, J_{C-P} = 21.9 Hz), 154.8 (br), 141.9 (t, J_{C-P} = 20.7 Hz), 135.3, 134.8 (dt, J_{C-P} = 42.2, 4.8 Hz), 131.1 (d, J_{C-P} = 9.2 Hz), 129.9 (dt, J_{C-P} = 62.9, 20.5 Hz), 129.1 (dt, J_{C-P} = 16.9, 4.6 Hz), 127.6, 125.2, 38.2, 37.5 (t, J_{C-P}= 12.3 Hz), 34.4, 30.2, 27.9 (m), 27.0; ^{31}P NMR (121 MHz, C_6D_6) δ 32.1; IR (KBr) 3447, 3059, 3036, 2994, 2930, 2849, 2162, 1553, 1483, 1431, 1352, 1260, 1175, 1159, 1071, 1044, 1030, 999, 916, 887, 860, 853, 806, 745, 729, 700,

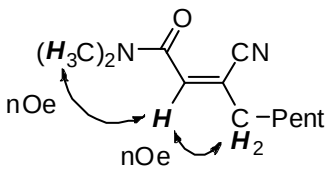


662, 638, 617, 527, 515 cm^{-1}.

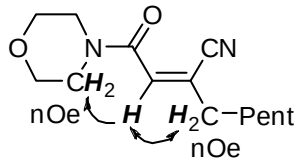
Desilylation of 23. ***A general procedure*****.**

To a solution of **23** (0.100 mmol) in THF (3.0 mL) were added CF_3CO_2H (31 mg, 0.27 mmol) and a 1.0 M solution of TBAF (0.40 mL, 0.40 mmol) in THF successively at 0 °C. The resulting reaction mixture was stirred at 0 °C for 3 h. The reaction was quenched with water, and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give corresponding desilylated products.

(*Z*)-3-cyano-*N*,*N*-dimethylnon-2-enamide. A colorless oil, R_f 0.25 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (t, *J* = 1.3 Hz, 1H), 3.07 (s, 3H), 3.04 (s, 3H), 2.35 (td, *J* = 7.6, 1.2 Hz, 2H), 1.62 (quint, *J* = 7.2 Hz, 2H), 1.40–1.22 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 134.3, 122.9, 116.5, 37.6, 35.5, 35.3, 31.4, 28.4, 27.6, 22.6, 14.1; IR (neat): 2955, 2930, 2859, 2218, 1657, 1651, 1645, 1622, 1495, 1462, 1456, 1416, 1402, 1261, 1171, 1138, 1096, 1059, 891, 727, 629, 579 cm^{-1}. Anal. Calcd for $C_{12}H_{20}N_2O$; C, 69.19; H, 9.68. Found: C, 69.20; H, 9.57.



***N*-[(*Z*)-2-Cyanonon-2-enoyl]morphiline.** A white solid, mp 51.9–52.2 °C, R_f 0.18 (hexane–ethyl acetate = 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (t, *J* = 1.4 Hz, 1H), 3.72 (br s, 6H), 3.51 (br t, *J* = 4.8 Hz, 2H), 2.36 (td, *J* = 7.6, 1.3 Hz, 2H), 1.70–1.56 (m, 2H), 1.42–1.22 (m, 6H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 133.7, 123.4, 116.4, 66.6, 46.7, 42.2, 35.4, 31.4, 28.5, 27.6, 22.6, 14.1; IR (neat): 3059, 2961, 2920, 2857, 2214, 1643, 1620, 1460, 1445, 1385, 1356, 1331, 1296, 1271, 1244, 1111, 1071, 1040, 1011, 999, 980, 964, 922, 907, 889, 872, 854, 827, 799, 785, 739, 714, 679, 629, 598, 575 cm^{-1}. Anal. Calcd for $C_{14}H_{22}N_2O_2$; C, 67.17; H, 8.86. Found: C, 67.07; H, 8.87.

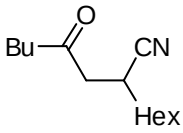


***N*-[(*E*)-2-Cyanonon-2-enoyl]morphiline.** A pale yellow oil, R_f 0.25 (hexane–ethyl acetate = 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (s, 1H), 3.73–3.61 (m, 6H), 3.44 (t, *J* = 4.8 Hz, 2H), 2.36 (t, *J* = 7.4 Hz, 2H), 1.59 (quint, *J* = 5.7 Hz, 2H), 1.40–1.22 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 134.9, 124.4, 118.0, 66.61, 66.59, 46.5, 41.8, 31.4, 30.6, 28.6, 27.8, 22.5, 14.1; IR (KBr): 2959, 2928, 2859, 2220, 1651, 1643, 1634, 1462, 1454, 1441, 1435, 1362, 1300, 1273, 1240, 1194, 1115, 1069, 1045, 1017, 972, 924, 853 cm^{-1}. Anal. Calcd for $C_{14}H_{22}N_2O_2$; C, 67.17; H, 8.86. Found: C, 67.15; H, 8.63.

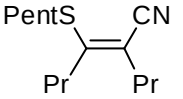
Hydrogenation of *N*-[(*Z*)-2-Cyanonon-2-enoyl]morphiline. To a suspension of Pd on carbon (5wt%, 107 mg, 0.050 mmol) in dioxane (2.5 mL) were added the title substrate (125 mg, 0.50 mmol) at room temperature, and the resulting reaction mixture was stirred at room temperature for 5 h under a hydrogen atmosphere before dilution with diethyl ether. Filtration of the insoluble materials through a Celite pad and concentration of the filtrate *in vacuo* gave *N*-(3-cyanononanoyl)morphiline (**29**, 125 mg, 99%) as a colorless oil, R_f 0.10 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76–3.54 (m, 6H), 3.52–3.38 (m, 2H), 3.17 (quint, *J* = 7.0 Hz, 1H), 2.73 (dd, *J* = 16.0, 7.3 Hz, 1H), 2.50 (dd, *J* = 16.0, 6.4 Hz, 1H), 1.64–1.22 (m, 10H), 0.89 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 121.9, 66.8, 66.4, 45.8, 42.2, 35.6, 32.3, 31.6, 28.7, 27.8, 27.2, 22.6, 14.1; IR (neat): 2957, 2928, 2859, 2239, 1657, 1651, 1643, 1462, 1445, 1362, 1300, 1273, 1235, 1117, 1071, 1034, 961, 851, 725, 579 cm^{-1}. Anal. Calcd for $C_{14}H_{24}N_2O_2$; C, 66.63; H, 9.59. Found: C, 66.46; H, 9.33.

Reaction of 29 with *n*-BuLi. A 1.6 M solution of *n*-BuLi in hexane was added to a solution of **29** (25 mg, 0.100 mmol) in THF (0.50 mL) at –78 °C, and the resulting mixture was stirred at –78 °C for 0.5 h before quenching with a saturated NH_4Cl aqueous solution. The mixture was extracted with diethyl ether for 3 times. The combined organic layers were washed successively with a 1M HCl aqueous solution and then with brine, dried over anhydrous magnesium sulfate, and concentrated *in*

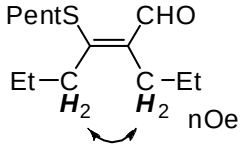
vacuo. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 15 : 1 as an eluent) to give 7-cyano-4-tridecanone (**30**, 10.5 mg, 47%) as a colorless oil, R_f 0.15 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (quint, *J* = 6.9 Hz, 1H), 2.82 (dd, *J* = 17.7, 7.0 Hz, 1H), 2.64 (dd, *J* = 17.7, 6.6 Hz, 1H), 2.44 (td, *J* = 7.5, 3.2 Hz, 2H), 1.68–1.20 (m, 14H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.0, 121.7, 44.6, 42.8, 31.9, 31.6, 28.7, 27.2, 26.1, 25.8, 22.6, 22.4, 14.1, 13.9; IR (neat): 2959, 2930, 2861, 2239, 1717, 1466, 1458, 1412, 1379, 1260, 1128, 1030, 802, 725 cm^{-1}. Anal. Calcd for $C_{14}H_{25}N_2O$; C, 75.28; H, 11.28. Found: C, 75.08; H, 11.15.



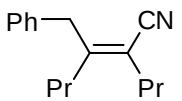
Palladium/$B(C_6F_5)_3$-catalyzed decarbonylative thiocyanation of 4-octyne. In a dry box, *S*-pentyl cyanomethanethioate (**31**, 157 mg, 1.00 mmol), 4-octyne (**2a**, 110 mg, 1.00 mmol), and tetradecane (internal standard, 99 mg, 0.50 mmol) were added sequentially to a solution of PdCp(π-allyl) (10.6 mg, 50 μmol), $B(C_6F_5)_3$ (134 mg, 0.20 mmol), and $P(4\text{-}CF_3\text{–}C_6H_4)_3$ (47 mg, 0.10 mmol) in toluene (2.0 mL) placed in a vial. The vial was closed and taken outside the dry box and heated at 100 °C for 24 h. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash column chromatography on silica gel to give (*Z*)-3-pentylthio-2-propylhex-2-enenitrile (**32**, 0.24 g, quant) as a pale yellow oil, R_f 0.18 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79 (t, *J* = 7.4 Hz, 2H), 2.34 (t, *J* = 7.7 Hz, 2H), 2.24 (t, *J* = 7.5 Hz, 2H), 1.66–1.50 (m, 6H), 1.45–1.27 (m, 4H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 118.4, 112.1, 33.5, 33.0, 32.2, 30.9, 29.5, 22.3, 22.2, 21.9, 14.0, 13.9, 13.6; IR (neat): 2961, 2932, 2872, 2203, 1574, 1518, 1379, 1343, 1323, 1298, 1275, 1252, 1171, 1109, 1088, 1061, 1016, 924, 889, 770, 733 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{25}NS$: M^+, 239.1708. Found: *m*/*z* 239.1708. The regiochemistry has been assigned based on ^{1}H nOe of (*Z*)-3-pentylthio-2-propylhex-2-enal (*vide infra*).



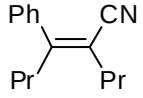
Reduction of 32 with DIBAL-H. To a solution of **32** (24 mg, 0.100 mmol) in toluene (1.00 mL) was added a 1.5 M solution of DIBAL–H in toluene (0.167 mL, 0.25 mmol) at –78 °C, and the resulting mixture was stirred at –78 °C for 1 h before quenching with MeOH at –78 °C. The mixture was warmed at room temperature, diluted with CH_2Cl_2, and filtered through a glass filter. The filtrate was concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 50 : 1 as an eluent) to give (*Z*)-3-pentylthio-2-propylhex-2-enal (11.3 mg, 54%) as an pale yellow oil, R_f 0.18 (hexane–ethyl acetate = 20 : 1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.3 (s, 1H), 2.73 (t, *J* = 7.3 Hz, 2H), 2.49 (t, *J* = 7.8 Hz, 2H), 2.30 (t, *J* = 7.9 Hz, 2H), 1.72–1.50 (m, 4H), 1.46–1.26 (m, 6H), 1.01 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 158.6, 141.4, 34.7, 32.3, 30.9, 29.6, 29.1, 22.8, 22.7, 22.3, 14.3, 14.2, 14.1; IR (neat) 2961, 2930, 2872, 1667, 1566, 1464, 1379, 1261, 1221, 1119, 1086, 1061, 1045, 1018, 924, 893, 872, 804, 758 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{26}OS$: M^+, 242.1704. Found: *m/z* 242.1697.



Nickel-catalyzed cross-coupling reaction of 32 with benzylmagnesium bromide.[8] A 2.0 M solution of benzylmagnesium bromide (0.40 mL, 0.80 mmol) in THF was added slowly to a solution of $NiCl_2(PPh_3)_2$ (26 mg, 0.020 mmol) and **32** (48 mg, 0.20 mmol) in THF (3.0 mL) at room temperature, and the resulting mixture was stirred at the 75 °C for 24 h before quenching with water. The mixture was extracted for three times with diethyl ether. The combined organic layers were washed successively with water and brine, dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane–ethyl acetate = 30 : 1 as an eluent) to give (*Z*)-3-benzyl-2-propylhex-2-enenitrile (**33**, 45 mg, 99%) as a pale yellow. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (tt, *J* = 7.1, 1.5 Hz, 2H), 7.27–7.19 (m, 3H), 3.74 (s, 2H), 2.24 (t, *J* = 7.6 Hz, 2H), 2.04 (t, *J* = 8.0 Hz, 2H), 1.63 (sext, *J* = 7.5 Hz, 2H), 1.38 (sext, *J* = 7.6 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 137.8, 128.7, 128.6, 126.7, 119.6, 111.2, 42.0, 32.7, 31.6, 21.8, 21.3, 14.1, 13.5

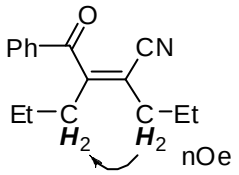


Palladium/BPh_3-catalyzed decarbonylative phenylcyanation of 4-octyne.[4a,b] In a dry box, benzoyl cyanide (**34**, 119 mg, 1.00 mmol), 4-octyne (**2a**, 110 mg, 1.00 mmol), and tetradecane (internal standard, 99 mg, 0.50 mmol) were added sequentially to a solution of PdCp(π-allyl) (10.6 mg, 0.050 mmol), BPh_3 (48 mg, 0.20 mmol), and $PCyPh_2$ (27 mg, 0.10 mmol) in toluene (2.0 mL) placed in a sealed tube. The sealed tube was closed and taken outside the dry box and heated at 100 °C for 24 h. The resulting mixture was filtered through a silica gel pad. The filtrate was concentrated *in vacuo* to give a residue, which was purified by flash column chromatography on silica gel, and



(*Z*)-3-phenyl-2-propylhex-2-enenitrile (**36**, 124 mg, 58%) was isolated as a pale yellow oil.

(*Z*)-3-Benzoyl-2-propylhex-2-enenitrile (35). A colorless oil, R_f 0.15 (hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.63 (td, *J* = 7.4, 1.4 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 2H), 2.50 (t, *J* = 7.9 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.72 (sext, *J* = 7.4 Hz, 2H), 1.47 (sext, *J* = 7.5 Hz, 2H), 1.06 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.2, 156.6, 134.9, 134.1, 129.4, 128.8, 171.1, 113.8, 33.1, 31.8, 21.5, 21.3, 14.2, 13.7; IR (neat): 2965, 2934, 2874, 2214, 1667, 1597, 1580, 1462, 1451, 1317, 1290, 1234, 1177, 1111, 1022, 1001, 974, 909, 721, 691 cm^{-1}. Anal. Calcd for $C_{16}H_{19}NO$; C, 79.63; H, 7.94. Found: C, 79.36; H, 7.99.



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Chapter 5

Cyanoesterification of 1,2-Dienes Catalyzed by Nickel

Cyanoformate esters add across 1,2-dienes in the presence of a nickel/PMe_2Ph catalyst to regioselectively afford β-cyano-α-methylenealkanoates, which are kinetically favored adducts and readily isomerize to thermodynamically favored α-cyanomethyl-α,β-unsaturated carboxylates at high temperature under the nickel catalysis, possibly through oxidative addition of the C–CN bond. Similar cyanoesterification products are produced from chloroformate esters, trimethylsilyl cyanide, and 1,2-dienes in the presence of a nickel/dppp catalyst. The resulting cyanoesterification products have the structure of allylic cyanide and thus undergo further allyl cyanation reaction across alkynes with the aid of a nickel/$P(4\text{-}CF_3\text{–}C_6H_4)_3$ catalyst to afford highly substituted acrylonitrile derivatives.

Introduction

Nickel or nickel/Lewis acid-catalyzed carbocyanation reactions of alkynes allows to introduce cyano and organic groups simultaneously through direct cleavage of C–CN bonds followed by insertion of alkynes to give highly substituted acrylonitriles with high regio- and stereoselectivities.[1] The carbocyanation of alkenes should also be an attractive method for preparation of various alkanenitriles. However, the alkene functionalization suffers from reluctant reductive elimination of C(sp^3)–CN bonds and competes with β-hydride elimination.[2] Accordingly, examples of this transformation involve intramolecular reactions[3,4] and intermolecular reactions across strained alkenes such as norbornene,[2,5] all relying on alkylnickel intermediates having no chance for β-hydride elimination. The author therefore envisioned use of 1,2-dienes as an alkene surrogate. Insertion of the double bond of 1,2-dienes into C–M bonds often results in π-allylmetal intermediates, which are reluctant to undergo β-hydride elimination.[1g,6] He reports herein realization of the carbocyanation of 1,2-dienes with cyanoformate esters to afford variously substituted β-cyano-α-methylenealkanoates.[7] He demonstrates that initially formed kinetic adducts isomerize to thermodynamically favored adducts through oxidative addition of the C–CN bonds, and performs the regiocontrol by simply changing the molar ratio of nitriles to 1,2-dienes and reaction temperature. He also shows that 1,2-diene-cyanoestefication products bearing various alkoxycarbonyl groups can be synthesized alternatively by nickel-catalyzed three-component coupling reaction of chloroformate esters, 1,2-dienes, and trimethylsilyl cyanide. Synthetic transformations of the resulting β-cyano-α-methylenealkanoates including allylcyanation reaction of alkynes are also demonstrated briefly.

Result and Discussion

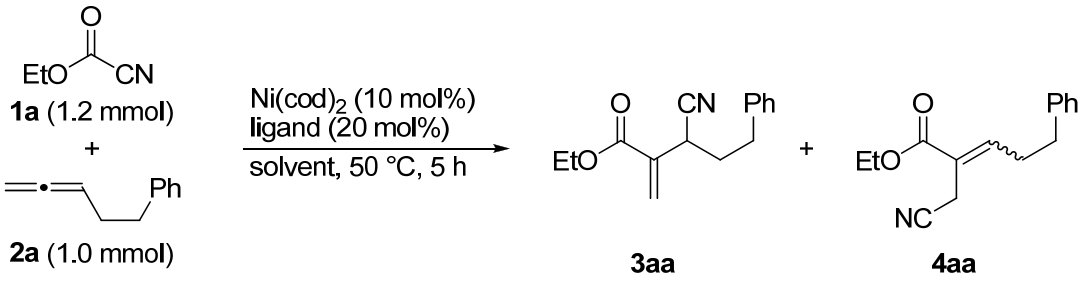
Nickel-catalyzed cyanoesterification of 1,2-dienes

The author first examined the reaction of ethyl cyanoformate (**1a**, 1.2 mmol) with 5-phenyl-1,2-pentadiene (**2a**, 1.0 mmol) in toluene at 50 °C in the presence of a catalyst prepared in situ from $Ni(cod)_2$ (0.10 mmol) and various phosphine ligands (Table 1). Oligomerization of **2a** was predominant, when trialkyl phosphine ligands such as PMe_3, PBu_3, PCy_3, or P*t*-Bu_3 were employed (entries 1–4). After thorough screening, PMe_2Ph

was found to be the most effective for the desired cyanoesterification reaction to give ethyl 3-cyano-2-methylene-5-phenylpentanoate (**3aa**) and (*Z*)-ethyl 2-(cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-**4aa**] in 77% and 10% yield, respectively (entry 5). Comparable yields of **3aa** and **4aa** were also obtained with $PMePh_2$ (entry 6), whereas PPh_3 and DPPP as well as the use of such polar solvents as DMF and 1,4-dioxane retarded the reaction (entries 7–10). While the ratio of **3aa** to **4aa** did not change after prolonged reaction time and/or at higher temperature, it was reversed by changing the molar ratio of **1a** : **2a** to 1.0 : 1.2 and by running reaction at 50 °C for 3 h then at 100 °C for 24 h to afford a stereoisomeric mixture of **4aa** as a major product (entry 11). These data provide with mechanistic insights including the reversibility of reductive elimination and relative thermodynamic stability of **3aa** and **4aa**. $Pd(PPh_3)_4$, a catalyst of choice for the cyanoesterification of norbornene and norbornadiene,[5] was completely ineffective for the reaction across 1,2-dienes.

With the optimized catalyst in hand, the author next examined the scope of 1,2-dienes using ethyl cyanoformate (**1a**) (Table 2). While the addition reaction across allene (**2b**) was sluggish due to rapid oligomerization of **2b** under the present reaction conditions (entry 1), the reactions with monosubstituted allenes having primary, secondary, and tertiary alkyl groups all proceeded with good yields and regioselectivity (entries 2–4). Higher regioselectivity was observed with a bulkier alkyl group. Substitutents such as protected hydroxyl, cyano, *N*-phthalimidoyl, ester, and terminal double bond were tolerated the reaction conditions to give highly functionalized α-cyanomethylacrylate esters (entries 5–10). Diastereoselectivity observed with 4-siloxy-1,2-pentadiene **2h** was modest (80 : 20) (entry 7). To his surprise, the reaction with 1,2-diene derived from diethyl malonate **2k** showed low regioselectivity (entry 10). Benzyl cyanoformate (**1b**) also participated in the reaction with **2a** in an acceptable yield under the similar conditions (entry 11). Di-substituted 1,2-dienes such as 3-methyl-1,2-butadiene (**2l**) and 5,6-undecadiene (**2m**) also underwent the reaction albeit in modest yields (entries 12 and 13).

Table 1. Cyanoesterification of 5-phenyl-1,2-pentadiene (**2a**) using ethyl cyanoformate (**1a**).[a]

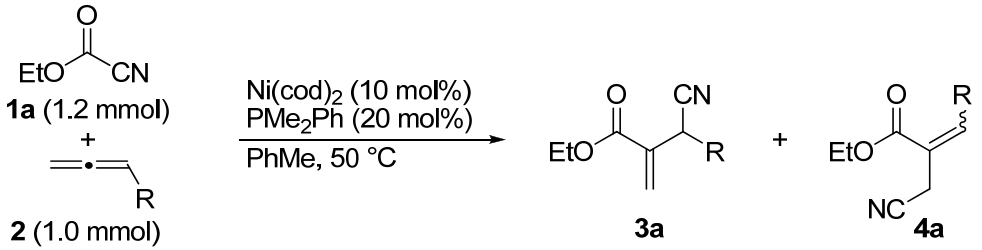


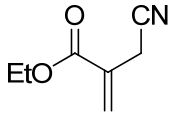
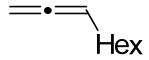
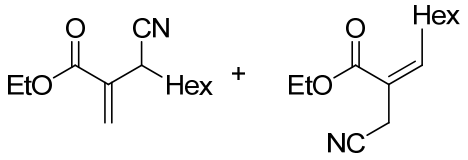
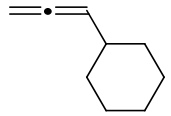
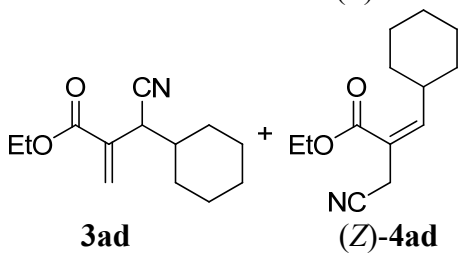
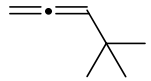
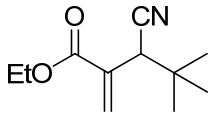
3aa **4aa**

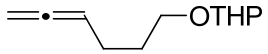
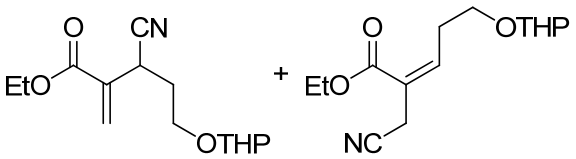
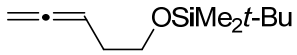
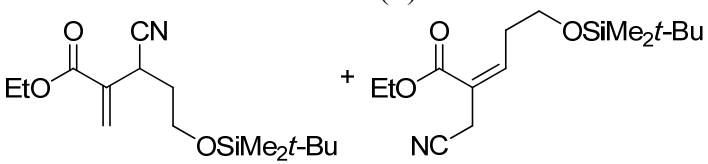
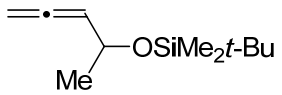
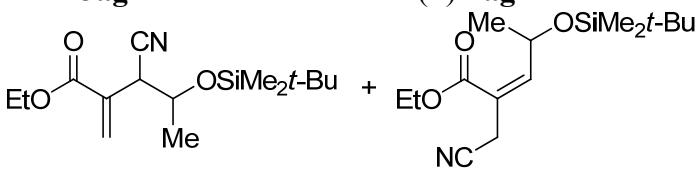
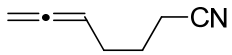
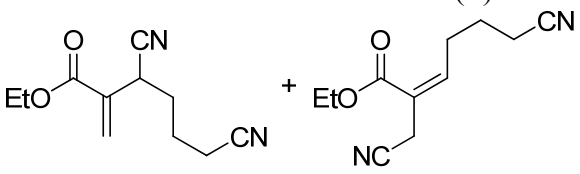
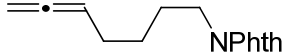
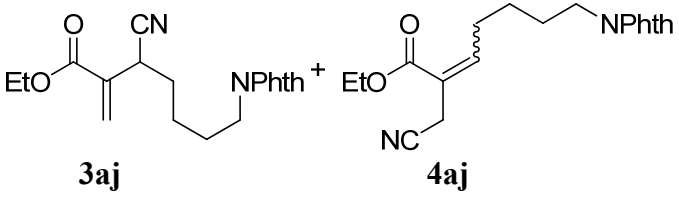
Entry	Ligand	Solvent	Yield of **3aa** (%)[b]	Yield of **4aa** (%) (*Z*:*E*) [b]
1	PMe_3	toluene	0	0
2	PBu_3	toluene	0	0
3	PCy_3	toluene	0	0
4	P*t*-Bu_3	toluene	0	0
5	PMe_2Ph	toluene	77[d]	10[d] (>95:5)[e]
6	$PMePh_2$	toluene	73	5 (>95:5)
7	PPh_3	toluene	7	2 (50:50)
8	DPPP[c]	toluene	18	3 (36:64)
9	PMe_2Ph	DMF	11	2 (>95:5)
10	PMe_2Ph	1,4-dioxane	23	4 (>95:5)
11[f]	PMe_2Ph	toluene	<5	78 [d] (17:83)[e]

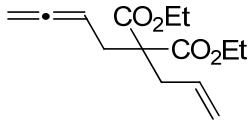
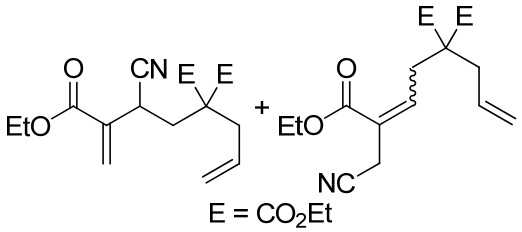
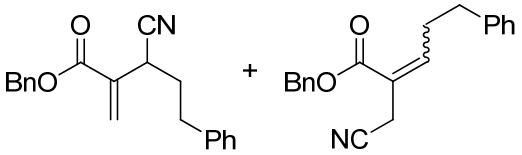
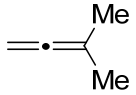
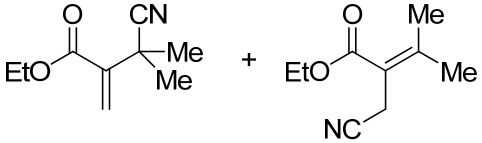
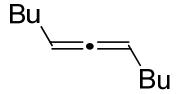
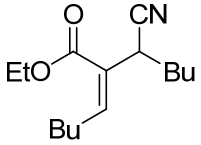
[a] All the reaction was carried out using **1a** (1.20 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and a ligand (0.20 mmol) in toluene (2.0 mL) at 50 °C. [b] Estimated by GC using tetradecane as an internal standard. [c] DPPP (0.100 mmol) was used. [d] Isolated yield. [e] Estimated by ^1H NMR analysis of an isolated product. [f] The reaction was carried out using **1a** (1.00 mmol) and **2a** (1.20 mmol) at 50 °C for 3 h and then at 100 °C for 24 h.

Table 2. Nickel-catalyzed cyanoesterification of 1,2-dienes.[a]



Entry	2	Time (h)	Products	Yield (%)[b] (**3a**:**4a**)[c]
1[d]	 **2b**	9	 **3ab**	17
2	 **2c**	5	 **3ac** (*Z*)-**4ac**	84 (89:11)
3	 **2d**	5	 **3ad** (*Z*)-**4ad**	93 (90:10)
4	 **2e**	6	 **3ae**	70 (>95:5)

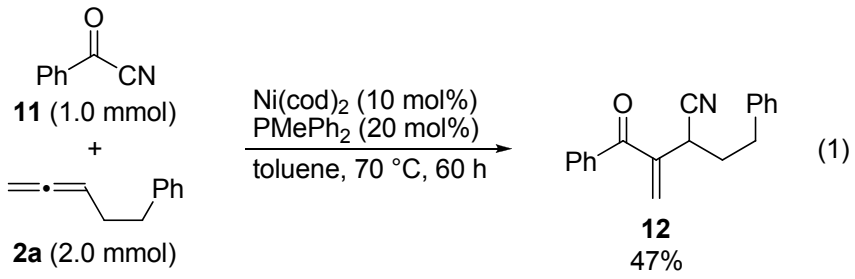
5	 **2f**	4	 **3af** (*Z*)-**4af**	75 (83:17)
6	 **2g**	5	 **3ag** (*Z*)-**4ag**	78 (82:18)
7	 **2h**	24	 **3ah** (*Z*)-**4ah**	74 (86[f]:14)
8	 **2i**	5	 **3ai** (*Z*)-**4ai**	79 (81:19)
9	 **2j**	4	 **3aj** **4aj**	91 [84:16 (*Z*:*E* = 90:10)][e]

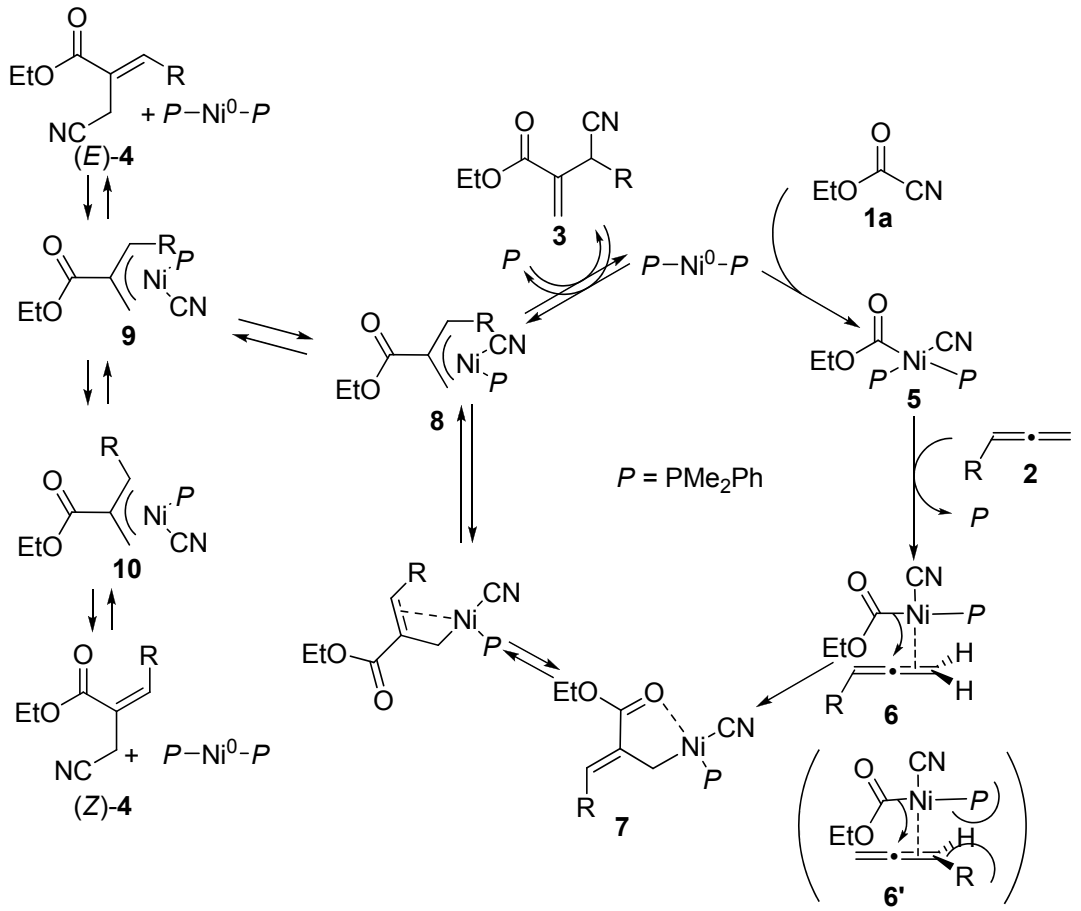
10	 **2k**	9	 **3ak** + **4ak**	59 [51:49 (*Z*:*E* = 42:58)][e]
11[g]	**2a**	18	 **3ba** + **4ba**	62 [82:18 (*Z*:*E* = 91:9)][e]
12	 **2l**	9	 **3al** + **4al**	61 (84:16)
13	 **2m**	24	 **3am**	45

[a] All the reaction was carried out using **1a** (1.20 mmol), **2** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and PMe_2Ph (0.20 mol) in toluene (2.0 mL) at 50 °C. [b] Isolated yield. [c] Calculated based on yields of isolated products. [d] The reaction was carried out under an atmosphere of **2b** (1 atm). [e] Estimated by ^1H NMR analysis of an isolated product. [f] dr = 80:20 as estimated by ^1H NMR analysis of an isolated product. Relative stereochemistry has not been identified. [g] The reaction was carried out using benzyl cyanoformate (**1b**, 1.00 mmol) instead of **1a**.

In a manner similar to other carbocyanation reactions, the cyanoesterification reaction should be initiated by oxidative addition of a EtOC(O)–CN bond to nickel(0) (Scheme 1).[5,8] The sterically less hindered terminal double bond of a 1,2-diene coordinates to the nickel center,[6a] and then the ethoxycarbonyl group migrates to a cumulative carbon of the coordinating 1,2-diene to give σ-allylnickel intermediate **7**, which isomerizes rapidly to π-allylnickel complex **8**. Reductive elimination finally produces **3** to regenerate nickel(0). Regioisomer **4** would be formed through coordination of 1,2-dienes in an opposite direction as shown in **6'** followed by similar steps involving π-allylnickel intermediates **9** or **10** under kinetically controlled conditions. Since **3** has an allyl cyanide substructure and oxidative addition of allyl cyanides to nickel(0) is feasible,[9] the reductive elimination, the product-forming step, would be reversible. Thus, under thermodynamically controlled conditions (entry 11 of Table 1), **3** undergoes further oxidative addition to nickel(0), isomerizaton of the resulting π-allylnickel **8** to **9** or **10**, and then reductive elimination to give (*E*)- or (*Z*)-**4**, which would be in equilibrium with **3**. The equilibrium should lead to (*E*)-**4** over **3** and (*Z*)-**4** after a longer reaction time at higher temperature, according to the relative order of their thermodynamic stability. Nevertheless, the presence of **1a** in excess (entry 5 of Table 1) would inhibit the oxidative addition of **3** because of the higher reactivity of **1a** than **3** toward oxidative addition of a C–CN bond to reduce the chance of **3** to isomerize even at elevated temperature.

Benzoyl cyanide (**11**) also regioselectivly added across **2a** in the presence of a nickel/$PMePh_2$ catalyst to give **12** in 47% yield as a sole product (eq. 1). No linear adducts were observed even at higher temperature.





Scheme 1. Plausible mechanism for the nickel-catalyzed cyanoesterification of 1,2-dienes.

Nickel-catalyzed cyanoesterification of 1,2-dienes by three-component coupling

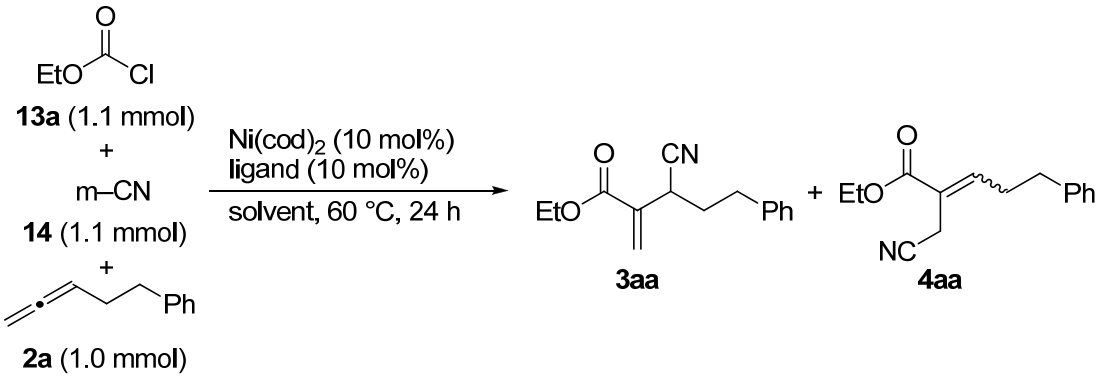
Cyanoformate esters are often synthesized from the corresponding chloroformate esters and metal cyanides such as KCN, NaCN, CuCN, and Me_3SiCN.[10] Therefore, a three-component coupling reaction of chloroformate esters, metal cyanides, and 1,2-dienes would be a practically straightforward way for the cyanoesterification of 1,2-dienes. To realize this alternative protocol, the author first examined the reaction of **2a** with ethyl chloroformate (**13a**) and trimethylsilyl cyanide (**14**) in toluene in the presence of $Ni(cod)_2$ (10 mol%) and PMe_2Ph (20 mol%) (entry 1 of Table 3) to observe formation of **3aa** and **4aa** in only a small amount. Because a mechanistic scenario for the three-component approach was possibly different from that for the direct cyanoesterfication initiated by the oxidative addition of cyanoformate esters, the author briefly examined the effect of other phosphine ligands, and found that nickel/dppp

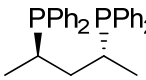
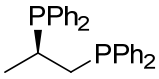
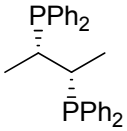
effectively catalyzed the three-component reaction to give **3aa** and a stereoisomeric mixture of **4aa** (entry 3). Other bidentate phosphine ligands with a different bite angle, DPPE and DPPB, showed inferior catalytic activity (entries 2 and 4). An electron-donating variant having dimethylphosphino groups completely retarded the reaction (entry 5). Chiral analogues of DPPP and DPPE were not effective (entries 6–8). Other metal cyanides such as KCN, CuCN, and $Zn(CN)_2$ were not effective in toluene or DMF even in the presence of a crown ether or a phase-transfer catalyst (entries 9–16).

With the nickel/dppp catalyst, the author next examined scope of the three-component cyanoesterification of **2a** and found that those having an internal triple bond, methoxyethyl, chloroethyl, and (–)-mentyl all participated in the three-component reaction (Table 4). To this regret, no diastereoselection (50 : 50) was attained with a optically pure chloroformate ester derived from **13e** (entry 4).

Scope of 1,2-dienes for the three-component strategy was found to be broad as is demonstrated in Table 5. Ethyl chloroformate (**13a**) and trimethylsilyl cyanide (**14a**) reacted with primary, secondary, and tertiary alkyl-substituted allenes in yields and with regioselectivity both comparable to the direct cyanoesterification (entries 1–3). Similar functional group tolerance was also observed (entries 4–9). The reaction with **3ah** shows the similar diastereoselectivity of the reaction using ethyl cyanoformate (entry 5). On the other hand, 1,2-dienes **2l** and **2n**–**2p** showed reversed regioselectivities (entries 9–12). Phenylallene (**2o**) and chiral *N*-allenyloxazolidinone **2p** were applicable to this three-component reaction, while no trace amount of the adducts was obtained in the direct cyanoesterification with ethyl cyanoformate (entries 10 and 11), although **2p** gave a linear adduct in a poor yield. No trace amount of adduct, however, was obtained with 5,6-dodecadiene (**2m**).

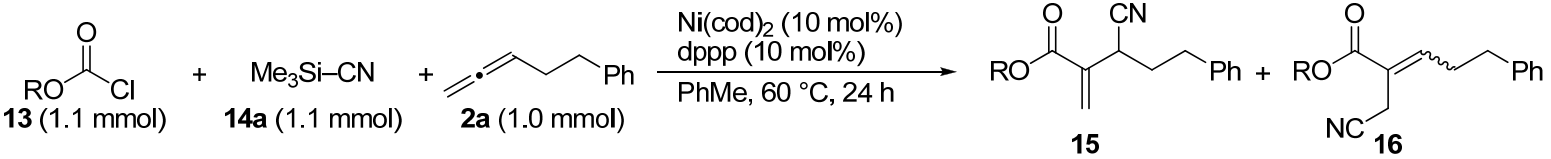
Table 3. Nickel-catalyzed cyanoesterification of **2a** by three-component coupling reaction.[a]

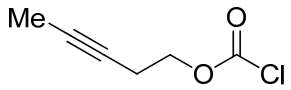
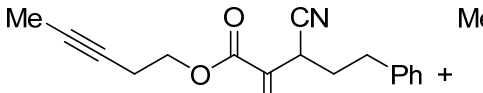
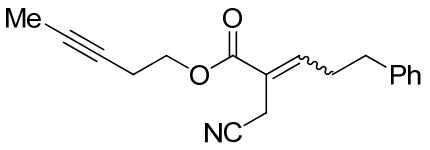
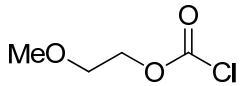
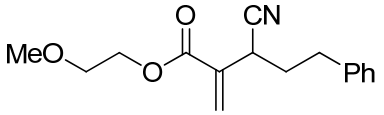
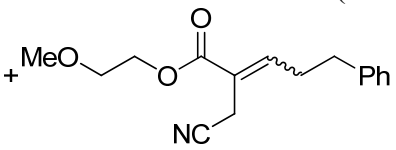
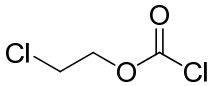
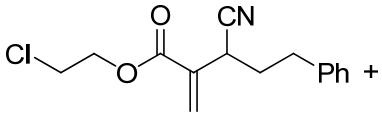
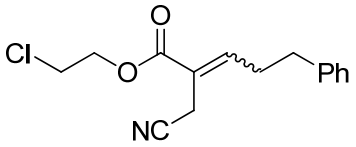
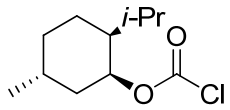
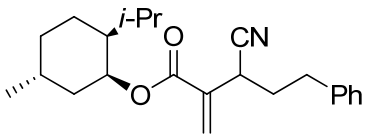
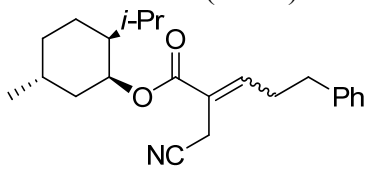


Entry	**14**	Ligand	Solvent	Yield of **3aa** (%)[b]	Yield of **4aa** (%) (*E*:*Z*)[b]
1	Me_3SiCN (**14a**)	PMe_2Ph[c]	toluene	1	5 (87:13)
2	**14a**	DPPE	toluene	56	26 (76:27)
3	**14a**	DPPP	toluene	78[d]	21[d] (62:38)[e]
4	**14a**	DPPB	toluene	9	11 (82:18)
5	**14a**	DMPP	toluene	0	0
6[f]	**14a**		toluene	0	0
7[f]	**14a**		toluene	0	0
8[f]	**14a**		toluene	0	0
9	KCN (**14b**)	DPPP	toluene	0	0
10	**14b**	DPPP	DMF	0	0
11[g]	**14b**	DPPP	DMF	0	0
12[h]	**14b**	DPPP	DMF	0	0
13	CuCN (**14c**)	DPPP	toluene	0	0
14	**14c**	DPPP	DMF	0	0
15	$Zn(CN)_2$ (**14d**)	DPPP	toluene	0	0
16	**14d**	DPPP	DMF	0	0

[a] All the reaction was carried out using **13a** (1.10 mmol), **14** (1.10 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and a ligand (0.100 mol) in toluene (0.67 mL). [b] Estimated by GC using tetradecane as an internal standard. [c] PMe_2Ph (0.20 mmol) was used. [d] Isolated yield. [e] Calculated based on yields of isolated products. [f] Reactions were carried out using **13a** (0.33 mmol), **14** (0.33 mmol), and **2a** (0.30 mmol). [g] 18-crown-6 (1.10 mmol) was used. [h] TBAB (1.10 mmol) was used.

Table 4. Nickel-catalyzed cyanoesterification of **2a** by three-component coupling reaction: Scope of chloroformate esters.[a]

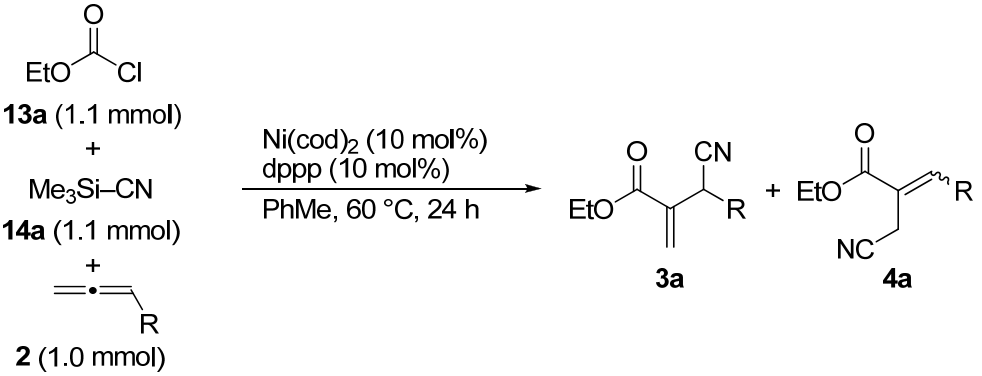


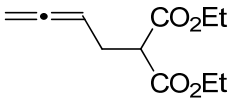
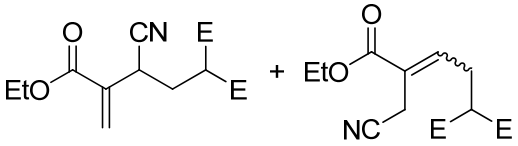
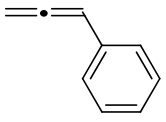
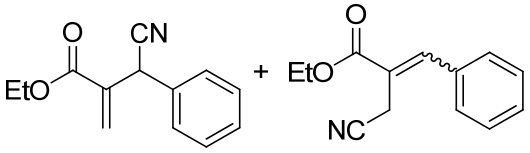
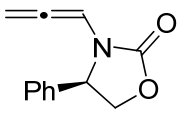
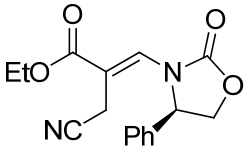
Entry	**13**	Products (*E*:*Z*)[b]	Yield (%),[c] (**15**:**16**)
1	 **13b**	 **15ba** +  **16ba** (75:25)	72 (61:39)
2	 **13c**	 **15ca** +  **16ca** (65:35)	69 (83:17)
3	 **13d**	 **15da** +  **16da** (72:28)	96 (81:19)
4	 **13e**	 **15ea** +  **16ea** (67:33)	75 (84[d]:16)

[a] All the reaction was carried out using **13** (1.10 mmol), **14a** (1.10 mmol), **2a** (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and dppp (0.100 mol) in toluene (0.67 mL). [b] Calculated based on isolated yields of (*E*)- and (*Z*)-**16**. [c] Isolated yield of **15** and **16**. [d] dr = 50:50 as estimated by ^{1}H NMR analysis of an isolated product.

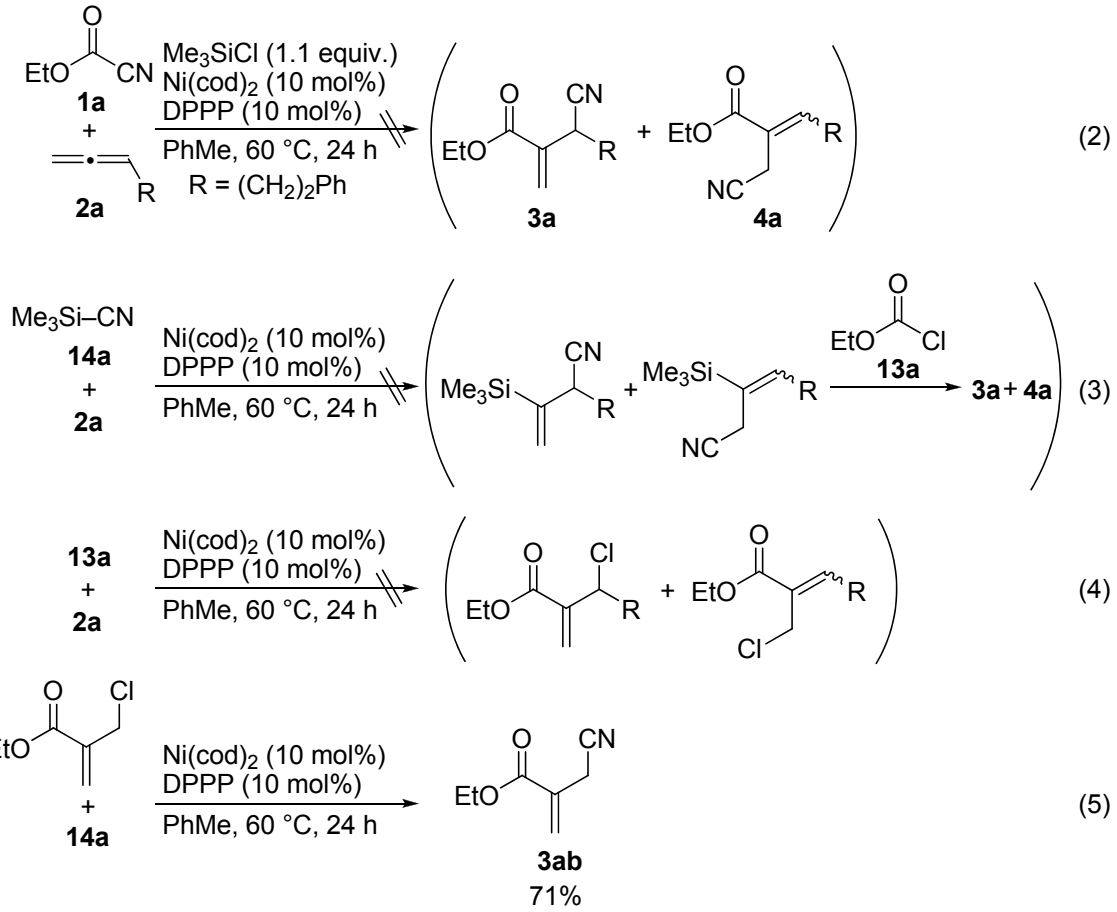
The following experiments were performed to gain a mechanistic insight into the three-component coupling reaction. The reaction of ethyl cyanoformate (**1a**) with **2a** in the presence of trimethylsilyl chloride did not proceed at all (eq. 2). This together with the observed poor activity of nickel/dppp for the reaction of **1a** with **2a** (entry 8 of Table 1) excludes a reaction path that go through in situ generation of **1a** from **13a** and **14a** and then its addition across 1,2-dienes. Alternative pathway may involve nickel-catalyzed silylcyanation of **2a**[11] followed by cross-coupling of the resulting alkenylsilanes with chloroformate esters. Because no silylcyanation of **2a** was observed with the nickel/dppp catalyst (eq. 3), this possibility can also be ruled out. Finally, a reaction sequence involving chloroesterification of 1,2-dienes[12] followed by cyanation of the resulting substituted allylic chloride was unlikely based on the fact that no chloroesterification products were obtained with the reaction of **13a** with **2a** under the nickel/dppp catalysis (eq. 4), though the reaction of ethyl α-chloromethylacrylate underwent cross-coupling reaction with **14a** in the presence of the nickel/dppp catalyst to give **3aj** in 71% yield (eq. 5).

Table 5. Nickel-catalyzed cyanoesterification of 1,2-dienes by three component coupling.[a]

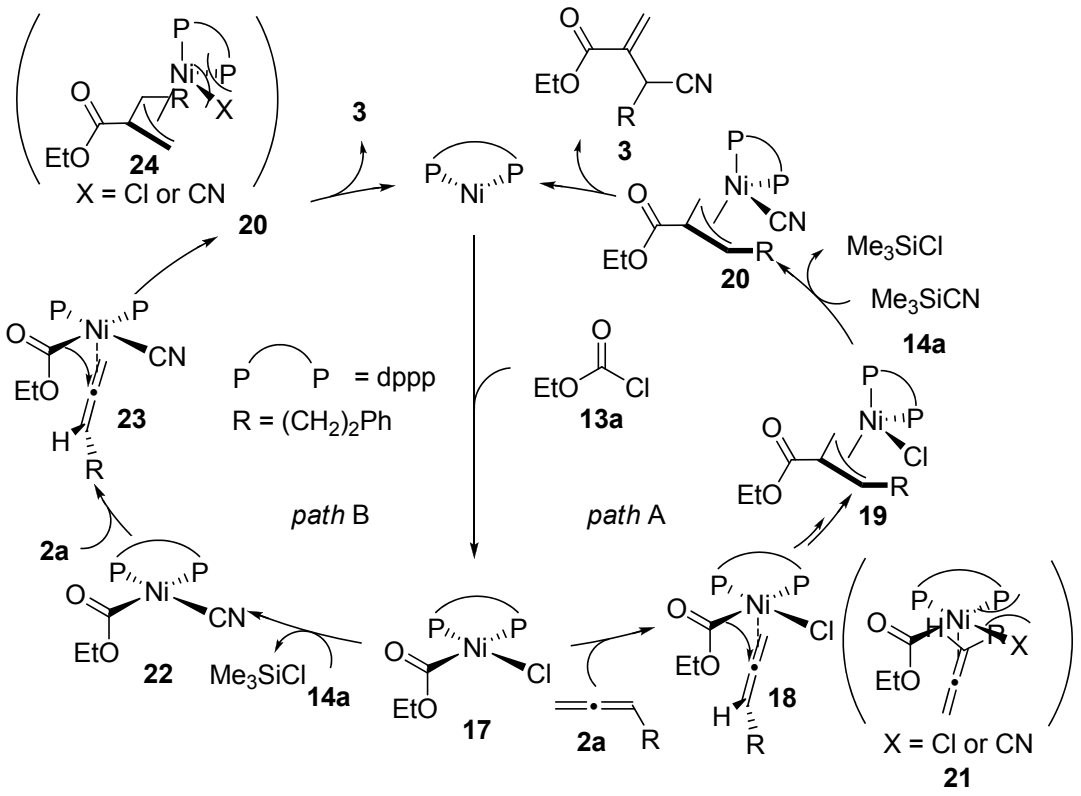


Entry	**2**	Products (*E*:*Z*)[b]	Yield (%),[c] (**3a**:**4a**)
1	**2c**	**3ac**, **4ac** (60:40)	84 (88:12)
2	**2d**	**3ad**, **4ad** (75:25)	84 (86:14)
3	**2e**	**3ae**, **4ae** (87:13)	77 (99:1)
4	**2g**	**3ag**, **4ag** (57:43)	81 (83:17)
5	**2h**	**3ah**, **4ah** (72:28)	84 (69[d]:31)
6	**2i**	**3ai**, **4ai** (50:50)	91 (80:20)
7	**2j**	**3aj**, **4aj** (60:40)	84 (85:15)
8	**2k**	**3ak, 4ak** (>95:5)	82 (49:51)
9	 **2n**	 E = CO_2Et **3an** **4an** (66:34)	80 (49:51)
10	 **2o**	 **3ao** **4ao** (87:13)	54 (13:87)
11	 **2p**	 (*E*)-**4ap** (>95:5)	28 (5:>95)
12	**2l**	**3al**, **4al** (17:83)	84 (17:83)

[a] All the reaction was carried out using **13a** (1.10 mmol), **14a** (1.10 mmol), a 1,2-diene (1.00 mmol), $Ni(cod)_2$ (0.100 mmol), and dppp (0.100 mol) in toluene (0.67 mL). [b] Calculated based on isolated yields of **4**. [c] Isolated yield of **3** and **4**. [d] dr = 81:19 as estimated by ^1H NMR analysis of an isolated product.



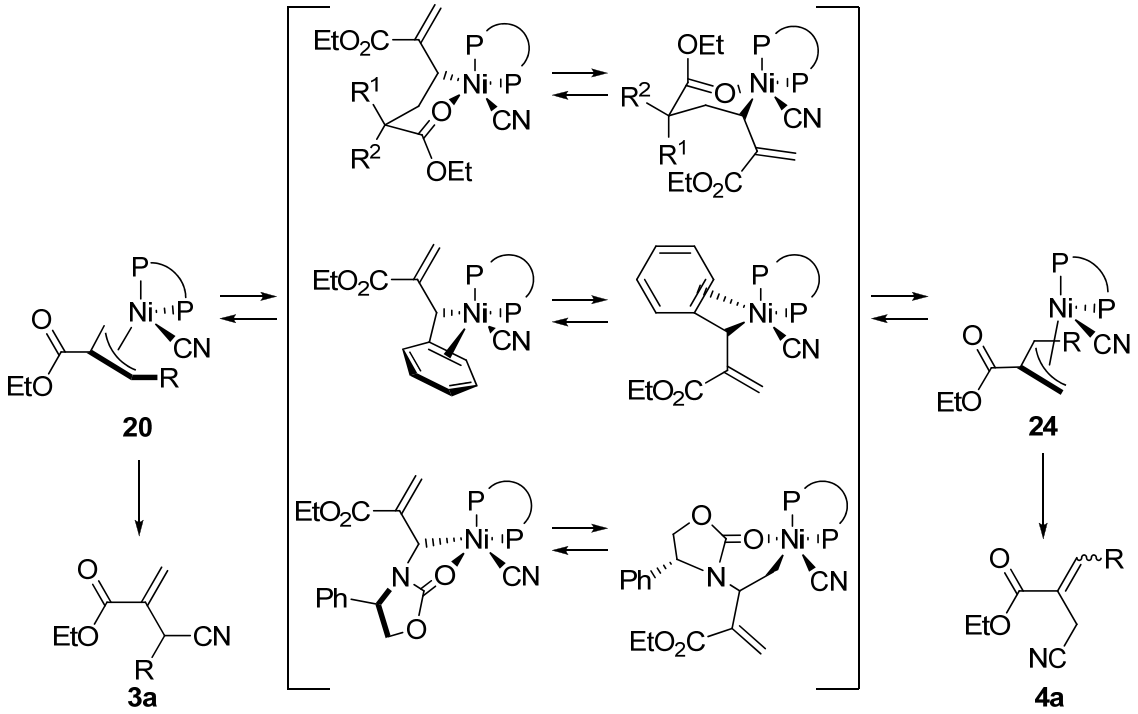
Based on these results, two reaction pathways (path A and path B) are suggested in Scheme 2. In each cycle, catalysis should be initiated by oxidative addition of a C–Cl bond in **13** to nickel(0) to give **17**. Subsequent coordination of 1,2-dienes to the nickel center in **17** would give **18** rather than **21** due to steric reason. Migratory insertion of the ethoxycarbonyl group on nickel affords π-allylnickel intermediate **19**, which undergoes transmetalation with **14a** to give π-allylnickel **20**. Reductive elimination of **20** gives **3** and regenerates nickel(0)/dppp (path A). Alternatively, transmetalation may precede to give **22**, which undergoes coordination followed by insertion of 1,2-dienes and reductive elimination (path B). Formation of regioiosmer **4** would be derived from such coordination of 1,2-dienes in an opposite direction as **21** or π-allylnickel intermediate **24**, both intermediates suffering from steric repulsion between a R group and the diphenylphosphino group.



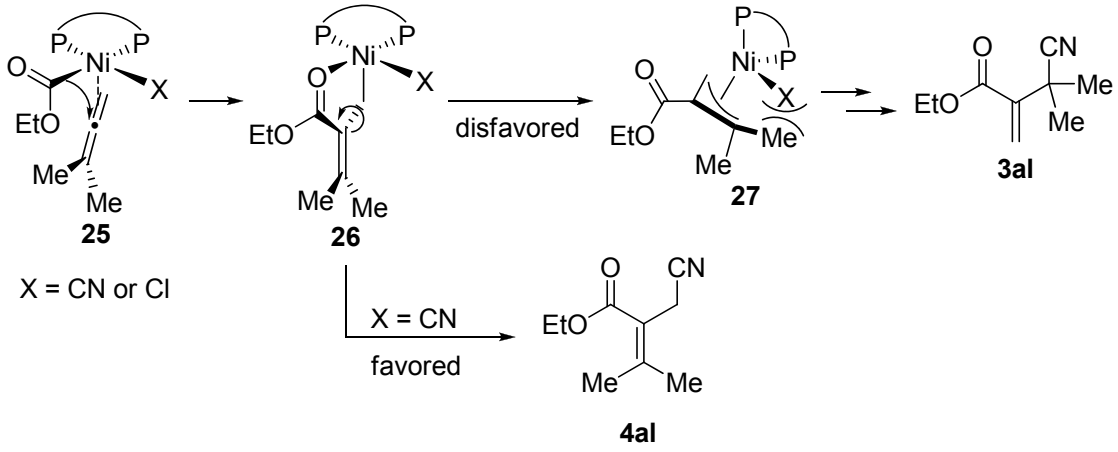
Scheme 2. Plausible mechanism of cyanoesterification of 1,2-dienes via three-component coupling.

With 1,2-dienes **2k** and **2n**–**2p**, reductive elimination from π-allylnickel intermediate **20** may be hampered by intramolecular coordination of carbonyl or phenyl groups (Scheme 3) to allow σ-π-σ isomerization to π-allynickel intermediates **24**, which reductively eliminate **4a** as a major product with these particular 1,2-dienes.

In the case of **2l**, the nickel center of 1,2-diene-coordinating nickel species **25** coordinated by two diphenylphosphino groups of DPPP (Scheme 4) would have a greater steric bulk compared with related intermediate **6** having a monophosphine ligand (Scheme 1). Therefore, migratory insertion followed by reductive elimination of **4al** from intermediate **26** would be favored rather than formation of π-allylnickel intermediate **27**, which should lead to **3al**.



Scheme 3. Plausible mechanism for the formation of **4** with **2k** and **2n**–**2p**.

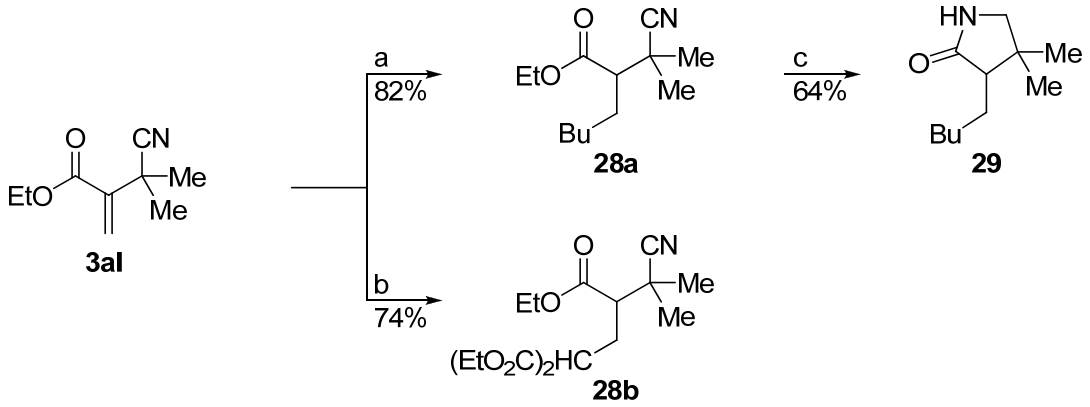


Scheme 4. Plausible mechanism for the formation of **4al** with **2l** through the three-component coupling.

Transformations of 1,2-diene-cyanoesterification products

The cyanoesterification products thus obtained have both α,β-unsaturated ester and allylic cyanide functionalities, which can be transformed orthogonally (Scheme 5). Cyanoesterification product **3al** derived from **1a** and **2l** underwent 1,4-addition reactions with butylcopper/BF_3•OEt_2[13] or sodium malonate to give the corresponding β-cyano esters **28a** and **28b**, respectively. Subsequent treatment of **28a** with $NaBH_4$ in

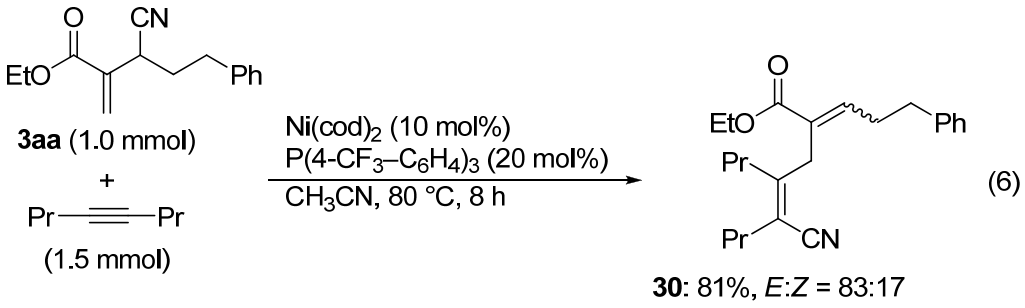
the presence of $CoCl_2$ afforeded γ-lactam **29** via reduction of the cyano group to aminomethyl followed by lactamization.[14]



Reagents and Conditions: (a) BuLi, CuI, BF_3•OEt_2, Et_2O, –70 °C to rt, 5 h; (b) $NaCH(CO_2Et)_2$, THF, 0 °C to rt, 1 h; (c) $NaBH_4$, $CoCl_2$, EtOH, 0 °C to rt, 9 h.

Scheme 5. Transformations of the cyanoesterification products.

The allylic cyanide moiety can participate in the carbocyanation reaction across alkynes. For example, cyanoesterification product **3aa** added across 4-octyne in the presence of a nickel/P(4-CF_3–C_6H_4)$_3$ catalyst to regioselectively give tri-substituted acrylonitrile **30** in 81% yield as a mixture of stereoisomers (eq. 6).[1d]



Conclusion

In conclusion, the author has demonstrated that cyanoformats add across 1,2-dienes regio- and stereoselectively in the presence of a nickel/PMe_2Ph catalyst, and, thus, have achieved regioselective preparation of variously functionalized β-cyano-α-methylene alkanoates. Cyanoesterification of 1,2-dienes has also been attained by a

three-component coupling of chloroformate esters, trimethylsilyl cyanide, and 1,2-dienes with the nickel/dppp catalyst as an alternative and convenient protocol to introduce various alkoxycarbonyl and cyano groups to 1,2-dienes in a single operation. The resulting cyanoesterification products would serve as synthetically useful building blocks for γ-aminobutyric acid, β-amino acids,[15] and 1,2-dicarboxylic acid derivatives.

Experimental section

Chemicals.

1,2-Dienes[16] and chloroformate ester (**13b**)[17] were prepared according to the respective literature procedure.

5-(2-Tetrahydro-2*H*-pyranoxy)-1,2-pentadiene (2f). A colorless oil, R_f 0.48 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (quint, J = 6.8 Hz, 1H), 4.70–4.64 (m, 2H), 4.63–4.56 (m, 2H), 3.92–3.83 (m, 2H), 3.83–3.75 (m, 2H), 3.56–3.42 (m, 2H), 2.35–2.26 (m, 2H), 1.88–1.76 (m, 1H), 1.75–1.66 (m, 1H), 1.66–1.46 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 208.9, 98.8, 86.7, 74.9, 66.8, 62.2, 30.6, 28.8, 25.4, 19.5; IR (neat) 2941, 1958, 1441, 1352, 1200, 1120, 1034, 980, 870 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.63; H, 9.83.

5-(*tert*-Butyldimethylsilyloxy)-1,2-pentadiene (2g). A colorless oil, R_f 0.13 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (quint, J = 7.0 Hz, 1H), 4.69–4.62 (m, 1H), 3.67 (t, J = 6.8 Hz, 2H), 2.27–2.18 (m, 2H), 0.90 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.0, 86.6, 74.5, 62.8, 32.0, 25.9, 18.3, –5.3; IR (neat) 2955, 2858, 1958, 1472, 1256, 1101, 937, 837, 775 cm^{-1}. Anal. Calcd for $C_{11}H_{23}OSi$: C, 66.60; H, 11.18. Found: C, 66.45; H, 11.21.

4-(*tert*-Butyldimethylsilyloxy)-1,2-pentadiene (2h). An yellow oil, R_f 0.38 (hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17 (q, J = 6.5 Hz, 1H), 4.82–4.70 (m, 2H), 4.43–4.13 (m, 1H), 1.28 (d, J = 6.2 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6, 96.2, 76.4, 67.2, 26.0, 24.6, 18.4, –4.4, –4.7; IR (neat) 2957, 2930, 2888, 2859, 1958, 1726, 1686, 1593, 1472, 1464, 1443, 1389, 1370, 1362, 1256, 1136, 1096, 1065, 988, 939, 880, 835, 812, 775, 667, 613, 575, 521 cm^{-1}; HRMS (EI) Calcd for $C_{11}H_{23}OSi$: $[M+H]^+$, 199.1518. Found: *m/z* 199.1517.

Nickel-catalyzed cyanoesterificaction of 1,2-dienes. ***A general procedure.***

In a dry box, ethyl cyanoformate (119 mg, 1.20 mmol) and a 1,2-diene (1.00 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and PMe_2Ph (27 mg, 0.20 mmol) in toluene (2.0 mL) placed in a vial. The vial was closed and taken outside the dry box, and heated at 50 °C for the time specified in Tables 1 and 2. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding cyanoesterification products in yields listed in Tables 1 and 2.

Ethyl 3-cyano-2-methylene-5-phenylpentanoate (3aa). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.28 (m, 3H), 7.25–7.19 (m, 2H), 6.47 (s, 1H), 6.07 (s, 1H), 4.29–4.18 (m, 2H), 3.81–3.74 (m, 1H), 2.95–2.86 (m, 1H), 2.83–2.73 (m, 1H), 2.20–2.09 (m, 1H), 2.07–1.96 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 139.6, 135.6, 128.6, 128.4, 127.9, 126.5, 119.6, 61.6, 34.3, 33.12, 33.10, 14.1; IR (neat) 2982, 2934, 2243, 1714, 1632, 1454, 1259, 1140, 1028, 960, 816, 750, 700 cm^{-1}; MS (EI) *m/z* (%) 243 (M^+, 17), 198 (19), 170 (12), 143 (24), 141 (35), 139 (68), 128 (10), 115 (36), 111 (69), 105 (60), 104 (24), 103 (15), 93 (19), 92 (16), 91 (100), 79 (14), 78 (14), 77 (20), 65 (21). Anal. Calcd for $C_{15}H_{17}NO_2$; C, 74.05; H, 7.04. Found: C, 74.12; H, 7.11.

Ethyl (*Z*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-4aa]. A colorless oil, R_f 0.18 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.24–7.18 (m, 3H), 6.45 (tt, J = 7.6, 1.3 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.31 (d, J = 1.3 Hz, 2H), 2.95 (q, J = 7.6 Hz, 2H), 2.79 (t, J = 7.6 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 147.1, 140.7, 128.5, 128.4, 126.2, 121.7, 117.2, 61.1, 34.9, 31.2, 22.6, 14.1; IR (neat) 2981, 2936, 2253, 1720, 1647, 1454, 1383, 1217, 1107, 1028, 750, 700 cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO_2$; C, 74.05; H, 7.04. Found: C, 73.75; H, 7.19.

Ethyl (*E*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*E*)-4aa]. A colorless oil, R_f 0.18 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.27–7.16 (m, 3H), 7.08 (t, *J* = 7.7 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.24 (s, 2H), 2.83 (t, *J* = 7.7 Hz, 2H), 2.60 (q, *J* = 7.7 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 146.2, 140.1, 128.6, 128.2, 126.4, 122.8, 116.9, 61.4, 34.1, 31.0, 14.9, 14.1; IR (neat) 2982, 2251, 1709, 1653, 1454, 1373, 1288, 1213, 1103, 748, 700 cm^{-1}. Anal. Calcd for $C_{15}H_{17}NO_2$; C, 74.05; H, 7.04. Found: C, 74.32; H, 7.25.

Ethyl 2-(cyanomethyl)acrylate (3ab). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (t, *J* = 1.3 Hz, 1H), 6.05 (t, *J* = 1.7 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 3.41 (t, *J* = 1.5 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 130.4, 128.2, 116.7, 61.7, 20.7, 14.1; IR (neat) 2986, 2942, 2909, 2253, 1722, 1715, 1641, 1470, 1447, 1418, 1371, 1331, 1302, 1281, 1260, 1221, 1150, 1115, 1096, 1024, 964, 858, 816, 689, 648 cm^{-1}. Anal. Calcd for $C_7H_9NO_2$; C, 60.42; H, 6.52. Found: C, 60.36; H, 6.62.

Ethyl 3-cyano-2-methylenenonanoate (3ac). A colorless oil, R_f 0.43 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (s, 1H), 6.04 (s, 1H), 4.32–4.19 (m, 2H), 3.83–3.75 (m, 1H), 1.85–1.62 (m, 2H), 1.60–1.22 (m, 11H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 135.9, 127.6, 120.0, 61.6, 33.5, 32.8, 31.4, 28.5, 26.9, 22.5, 14.1, 14.0; IR (neat) 2930, 2860, 2243, 1720, 1632, 1468, 1254, 1151, 1026, 959, 816 cm^{-1}. Anal. Calcd for $C_{13}H_{21}NO_2$; C, 69.92; H, 9.48. Found: C, 70.19; H, 9.35.

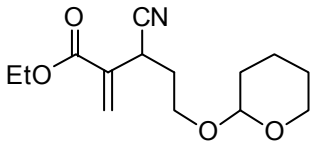
Ethyl (*Z*)-(2-cyanomethyl)non-2-enoate [(*Z*)-4ac]. A colorless oil, R_f 0.38 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (tt, *J* = 7.5, 1.3 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.34 (d, *J* = 1.3 Hz, 2H), 2.60 (q, *J* = 7.5 Hz, 2H), 1.50–1.10 (m, 2H), 1.37–1.22 (m, 9H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 148.7, 120.9, 117.4, 61.0, 31.5, 29.7, 29.0, 28.9, 22.7, 22.5, 14.1, 14.0; IR (neat) 2928, 2255, 1724, 1647, 1466, 1383,

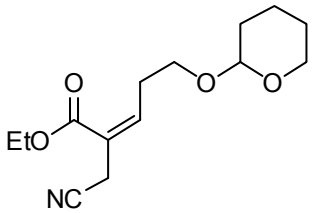
1213, 1142, 1096, 1024, 860 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{21}NO_2$: M^+, 223.1572. Found: *m*/*z* 223.1575.

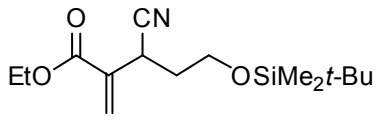
Ethyl 2-[cyano(cyclohexyl)methyl]acrylate (3ad). A colorless oil, R_f 0.43 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.47 (s, 1H), 5.99 (d, *J* = 0.8 Hz, 1H), 4.31–4.17 (m, 2H), 3.77 (dd, *J* = 4.9, 0.8 Hz, 1H), 1.86–1.61 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.30–1.02 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 134.5, 128.4, 119.1, 61.5, 40.1, 39.2, 31.6, 28.4, 26.0, 25.73, 25.69, 14.1; IR (neat) 2931, 2855, 2241, 1717, 1632, 1450, 1266, 1151, 1024, 959, 816 cm^{-1}. Anal. Calcd for $C_{13}H_{19}NO_2$; C, 70.56; H, 8.65. Found: C, 70.48; H, 8.59.

Ethyl (*Z*)-(2-cyanomethyl)-3-cyclohexylacrylate [(*Z*)-4ad]. A colorless oil, R_f 0.33 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.19 (d, *J* = 9.7 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.32 (s, 2H), 3.18–3.06 (m, 1H), 1.78–1.62 (m, 5H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.38–1.04 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.0, 153.3, 119.2, 117.4, 61.0, 38.2, 32.2, 25.7, 25.4, 22.7, 14.1; IR (neat) 2928, 2853, 2253, 1722, 1643, 1448, 1217, 1153, 1097, 1022, 978 cm^{-1}. Anal. Calcd for $C_{13}H_{19}NO_2$; C, 70.56; H, 8.65. Found: C, 70.68; H, 8.57.

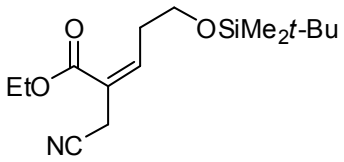
Ethyl 3-cyano-4,4-dimethyl-2-methylenepentanoate (3ae). A colorless oil, R_f 0.40 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.53 (s, 1H), 6.00 (s, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.03 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 134.7, 129.5, 119.9, 61.7, 43.0, 35.1, 26.9, 14.1; IR (neat) 2970, 2241, 1720, 1628, 1465, 1371, 1263, 1182, 1142, 1022, 961, 814 cm^{-1}; Anal. Calcd for $C_{11}H_{17}NO_2$; C, 67.66; H, 8.78. Found: C, 67.61; H, 8.59.

Ethyl 3-cyano-2-methylene-5-(2-tetrahydro-2*H*-pyranoxy)pentanoate (3af, mixture of diastereomers).  A colorless oil, R_f 0.33 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (s, 1H), 6.04 (s, 1H), 4.60 (t, *J* = 3,2 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.05–3.96 (m, 1H), 3.95–3.78 (m, 2H), 3.59–3.46 (m, 2H), 2.18–2.08 (m, 1H), 2.05–1.94 (m, 1H), 1.90–1.46 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 135.6, 128.1, 128.0, 119.61, 119.56, 99.1, 98.3, 64.0, 63.5, 62.3, 62.0, 61.5, 32.7, 32.6, 30.83, 30.80, 30.4, 30.3, 25.3, 19.3, 19.1, 14.1; IR (neat) 2943, 2871, 2243, 1720, 1632, 1369, 1261, 1202, 1136, 1036, 968, 870, 816 cm^{-1}. Anal. Calcd for $C_{14}H_{21}NO_4$; C, 62.90; H, 7.92. Found: C, 63.19; H, 8.21.

Ethyl (*Z*)-2-(cyanomethyl)-5-(2-tetrahydro-2*H*-pyranoxy)pent-2-enoate [(*Z*)-4af].  A colorless oil, R_f 0.25 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (t, *J* = 7.0 Hz, 1H), 4.60 (t, *J* = 3.5 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.89–3.80 (m, 2H), 3.56–3.46 (m, 2H), 3.36 (d, *J* = 1.3 Hz, 2H), 2.88–2.84 (m, 2H), 1.88–1.45 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 145.4, 122.3, 117.2, 98.8, 65.9, 62.3, 61.2, 30.5, 30.3, 25.4, 22.7, 19.5, 14.1; IR (neat) 2945, 2253, 1720, 1649, 1383, 1215, 1121, 1034, 986, 870, 814 cm^{-1}; HRMS (EI) Calcd for $C_{14}H_{21}NO_4$: M^+, 267.1471. Found: *m*/*z* 267.1467.

Ethyl 5-(*tert*-butyldimethylsiloxy)-3-cyano-2-methylenepentanoate (3ag).  A colorless oil, R_f 0.38 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (s, 1H), 6.02 (s, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 4.01 (dd, *J* = 9.6, 4.7 Hz, 1H), 3.71–3.84 (m, 2H), 1.98–2.09 (m, 1H), 1.93–1.73 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 135.8, 128.0, 119.7, 61.5, 59.6, 35.5, 30.3, 25.8, 18.2, 14.1, –5.5, –5.6; IR (neat) 2930, 2858, 2243, 1720, 1632, 1472, 1258, 1150, 1111, 951, 835, 777 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO_3Si$; C, 60.57; H, 9.15. Found: C, 60.52; H, 8.93.

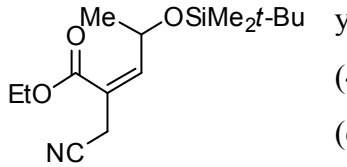
Ethyl (*Z*)-2-(cyanomethyl)-5-(*tert*-butyldimethylsiloxy)pent-2-enoate [(*Z*)-4ag]. A



colorless oil, R_f 0.23 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (tt, *J* = 7.0, 1.3 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.72 (t, *J* = 6.2 Hz, 2H), 3.35 (d, *J* = 1.4 Hz, 2H), 2.84 (dt, *J* = 7.0, 6.2 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 145.4, 122.1, 117.2, 61.7, 61.1, 33.2, 25.8, 22.7, 18.2, 14.1, –5.4; IR (neat) 2957, 2858, 2255, 1724, 1472, 1385, 1215, 1099, 837, 777 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO_3Si$; C, 60.57; H, 9.15. Found: C, 60.65; H, 9.01.

Ethyl 3-cyano-4-(*tert*-butyldimetylsiloxy)-2-methylenepentanoate [4ah, a mixture of diastereoisomers (80 : 20)]. A colorless oil, R_f 0.21 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$, as a mixture of diastereoisomers) δ 6.51 (s, 0.8H), 6.50 (s, 0.2H), 6.10 (s, 1H), 4.32–4.01 (m, 3H), 3.96 (dd, *J* = 5.1, 0.73 Hz, 0.8H), 3.83 (dd, *J* = 3.5, 0.92 Hz, 0.2H), 1.35 (d, *J* = 6.0 Hz, 0.6H), 1.331 (t, *J* = 7.1 Hz, 2.4H), 1.326 (t, *J* = 7.1 Hz, 0.6H), 1.22 (d, *J* = 6.0 Hz, 2.4H), 0.90 (s, 7.2H), 0.88 (s, 1.8H), 0.11 (s, 2.4H), 0.09 (s, 2.4H), 0.04 (s, 0.6H), –0.04 (s, 0.6H); ^{13}C NMR (101 MHz, $CDCl_3$, as a mixture of diastereoisomers) δ 164.7, 164.5, 133.2, 129.83, 129.77, 118.3, 117.9, 67.8, 67.3, 61.64, 61.56, 43.3, 43.0, 25.8, 25.7, 22.7, 20.1, 18.1, 18.0, 14.3, –4.4, –4.5, –4.75, –4.83; IR (neat, as a mixture of diastereoisomers) 2982, 2957, 2932, 2897, 2859, 2247, 1721, 1715, 1632, 1474, 1464, 1447, 1412, 1383, 1371, 1348, 1327, 1260, 1150, 1128, 1115, 1076, 1024, 1005, 972, 939, 905, 837, 810, 779, 683, 667 cm^{-1}. Anal. Calcd for $C_{15}H_{27}NO_3Si$; C, 60.57; H, 9.15. Found: C, 60.61; H, 8.93.

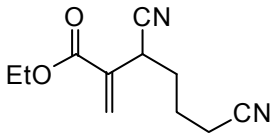
Ethyl (*Z*)-2-(cyanomethyl)-4-(*tert*-butyldimetylsiloxy)pent-2-enoate (3ah). A pale



yellow oil, R_f 0.08 (hexane–ethyl acetate = 20 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (dt, *J* = 7.7, 1.3 Hz, 1H), 5.30 (quint, *J* = 6.6 Hz, 1H), 4.33–4.20 (m, 2H), 3.34 (d, *J* = 0.73 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.27 (d, *J* = 6.4 Hz, 3H), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 152.8, 118.4, 116.8, 66.0, 61.5, 25.9,

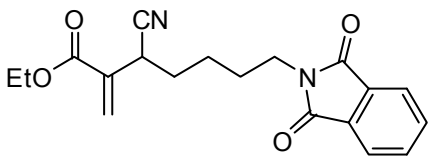
23.4, 22.5, 18.2, 14.3, –4.5, –4.6; IR (neat) 2957, 2930, 2888, 2859, 2255, 1722, 1715, 1651, 1472, 1464, 1447, 1416, 1379, 1294, 1254, 1227, 1148, 1125, 1088, 1003, 947, 939, 885, 833, 812, 777, 667 cm^{-1}; Anal. Calcd for $C_{15}H_{27}NO_3Si$; C, 60.57; H, 9.15. Found: C, 60.44; H, 8.91.

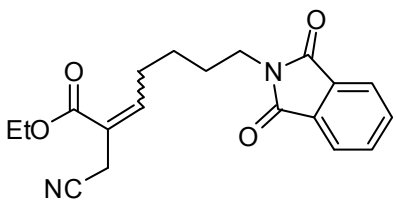
Ethyl 3,6-dicyano-2-methylenehexanoate (3ai). A colorless oil, R_f 0.20 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 1H), 6.08 (s, 1H), 4.32–4.19 (m, 2H), 3.85 (dd, *J* = 7.4, 4.7 Hz, 1H), 2.43 (t, *J* = 6.7 Hz, 2H), 2.04–1.74 (m, 4H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 134.9, 128.3, 119.0, 118.6, 61.8, 33.0, 31.4, 22.7, 16.6, 14.0; IR (neat) 2984, 2245, 1715, 1632, 1421, 1258, 1146, 1024, 964, 816 cm^{-1}. Anal. Calcd for $C_{11}H_{14}N_2O_2$; C, 64.06; H, 6.84. Found: C, 63.90; H, 6.86.

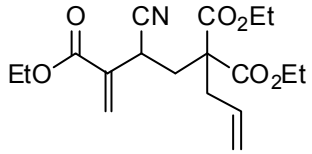


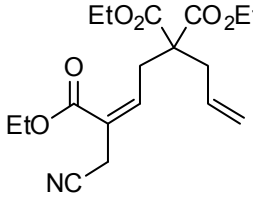
Ethyl (*Z*)-2-(cyanomethyl)-6-cyanohex-2-enoate [(*Z*)-4ai]. A colorless oil, R_f 0.14 (hexane–ethyl acetate = 2 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (tt, *J* = 7.7, 1.4 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.37 (d, *J* = 1.3 Hz, 2H), 2.76 (q, *J* = 7.7 Hz, 2H), 2.39 (t, *J* = 7.1 Hz, 2H), 1.84 (tt, *J* = 7.7, 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 144.6, 123.2, 119.1, 117.0, 61.4, 28.4, 24.6, 22.6, 16.8, 14.1; IR (neat) 2984, 2247, 1713, 1651, 1416, 1244, 1123, 1028 cm^{-1}. Anal. Calcd for $C_{11}H_{14}N_2O_2$; C, 64.06; H, 6.84. Found: C, 64.19; H, 6.88.

Ethyl 3-cyano-2-methylene-7-(*N*-phthalimidoyl)hepanoate (3aj). A colorless oil, R_f 0.21 (hexane–ethyl acetate = 3 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.82–7.71 (m, 2H), 7.70–7.60 (m, 2H), 6.38 (s, 1H), 5.98 (s, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.75 (dd, *J* = 8.8, 4.9 Hz, 1H), 3.65 (t, *J* = 7.0 Hz, 2H), 1.87–1.37 (m, 6H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 164.3, 135.4, 133.8, 131.8, 127.6, 123.0, 119.5, 61.4, 37.1, 33.2, 31.9, 27.6, 23.9, 13.9; IR (neat) 2939, 2866, 2243, 1771, 1713, 1633, 1396, 1371, 1259, 1152, 1047 cm^{-1}. Anal. Calcd for $C_{19}H_{20}N_2O_4$; C, 67.05; H, 5.92. Found: C, 67.14; H, 6.01.



Ethyl 2-(cyanomethyl)-7-*N*-phthalimdoylhept-2-enoate [4aj, a mixture of stereoisomers (*Z*/*E* = 90 : 10)].  A colorless oil, R_f 0.10 (hexane–ethyl acetate = 3 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.77 (m, 2H), 7.73–7.65 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 0.10H), 6.35 (t, *J* = 7.5 Hz, 0.90H), 4.22 (q, *J* = 7.1 Hz, 1.80H), 4.09 (q, *J* = 7.1 Hz, 0.20H), 3.58 (t, *J* = 7.1 Hz, 2H), 3.38 (s, 0.20H), 3.32 (d, *J* = 1.3 Hz, 1.80H), 2.64 (dt, *J* = 7.7, 7.5 Hz, 1.80H), 2.33 (dt, *J* = 7.7, 7.5 Hz, 0.20H), 1.76–1.64 (m, 2H), 1.58–1.42(m, 2H), 1.29 (t, *J* = 7.1 Hz, 2.70H), 1.23 (t, *J* = 7.1 Hz, 0.30H); ^{13}C NMR [for (*Z*)-**4aj**, 101 MHz, $CDCl_3$] δ 168.3, 164.8, 147.4, 133.8, 132.0, 123.1, 121.5, 117.2, 61.1, 37.5, 29.0, 28.2, 26.1, 22.6, 14.1; IR (neat, as a mixture of stereoisomers) 2939, 2864, 2253, 1773, 1715, 1396, 1375, 1215, 721 cm^{-1}; HRMS (EI) Calcd for $C_{19}H_{20}N_2O_4$: M^+, 340.1423. Found: *m*/*z* 340.1429.

Triethyl 3-cyanoocta1,7-diene-2,5,5-tricarboxylate (3ak).  A colorless oil, R_f 0.45 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (s, 1H), 6.05 (s, 1H), 5.74–5.60 (m, 1H), 5.23–5.10 (m, 2H), 4.32–4.13 (m, 6H), 3.89 (dd, *J* = 10.2, 3.8 Hz, 1H), 2.84 (dd, *J* = 14.5, 7.8 Hz, 1H), 2.73 (dd, *J* = 14.5, 7.2 Hz, 1H), 2.35 (dd, *J* = 14.8, 10.0 Hz, 1H), 2.27 (dd, *J* = 14.8, 4.0 Hz, 1H), 1.33 (t, *J* = 7.4 Hz, 3H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 164.2, 136.1, 131.4, 128.6, 120.1, 119.3, 61.82, 61.80, 61.7, 56.3, 37.0, 35.4, 29.0, 14.1, 13.94, 13.88; IR (neat) 2984, 2939, 2909, 2244, 1732, 1634, 1466, 1447, 1418, 1393, 1369, 1283, 1250, 1215, 1196, 1148, 1096, 1072, 1022, 968, 928, 862, 816, 667 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_6$; C, 61.52; H, 7.17. Found: C, 61.76; H, 7.26.

Triethyl (*Z*)-1-cyanoocta-2,7-diene-2,5,5-tricarboxylate [(*Z*)-4ak].  A colorless oil, R_f 0.35 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.41 (tt, *J* = 7.0, 1.3 Hz, 1H), 5.71–5.58 (m, 1H), 5.19–5.07 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 4H), 3.34 (d, *J* = 1.5 Hz, 2H), 3.19 (dt, *J* = 7.1, 1.3 Hz, 2H), 2.67 (d, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$)

δ 170.1, 164.6, 142.2, 131.8, 123.1, 119.5, 116.8, 61.6, 61.4, 56.9, 38.5, 33.1, 23.0, 14.25, 14.20. Anal. Calcd for $C_{18}H_{25}NO_6$; C, 61.52; H, 7.17. Found [as a mixture with (*E*)-**4ak**]: C, 61.77; H, 7.09.

Triethyl (*E*)-1-cyanoocta-2,7-diene-2,5,5-tricarboxylate [(*E*)-4ak]. A colorless oil, R_f 0.35 (hexane–ethyl acetate = 2 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (t, *J* = 7.6 Hz, 1H), 5.71–5.58 (m, 1H), 5.19–5.10 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 4H), 3.40 (s, 2H), 2.80 (d, *J* = 7.7 Hz, 2H), 2.70 (d, *J* = 7.3 Hz, 2H), 1.33 (t, *J* = 7.0 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 164.6, 140.9, 131.5, 124.7, 120.0, 116.5, 61.9, 61.7, 56.8, 37.9, 32.3, 15.6, 14.3, 14.2; IR (neat) 2984, 2940, 2909, 2253, 1730, 1713, 1655, 1466, 1445, 1414, 1391, 1325, 1368, 1300, 1275, 1211, 1144, 1096, 1065, 1017, 930, 860, 750 cm^{-1}.

Benzyl 3-cyano-2-methylene-5-phenylpentanoate (3ba). A colorless oil, R_f 0.23 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.14 (m, 10H), 6.51 (s, 1H), 6.11 (d, *J* = 1.0 Hz, 1H), 5.24 (d, *J* = 12.3 Hz, 1H), 5.19 (d, *J* = 12.3 Hz, 1H), 3.79 (ddd, *J* = 9.5, 4.8, 1.0 Hz, 1H), 2.94–2.83 (m, 1H), 2.82–2.70 (m, 1H), 2.20–2.08 (m, 1H), 2.06–1.94 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.3, 139.5, 135.4, 135.2, 128.7, 128.6, 128.5, 128.4, 128.3, 126.5, 119.5, 67.3, 34.2, 33.3, 33.1; IR (neat) 3030, 2932, 2243, 1720, 1631, 1497, 1454, 1259, 1136, 961, 750, 698 cm^{-1}. Anal. Calcd for $C_{20}H_{19}NO_2$; C, 78.66; H, 6.27. Found: C, 78.96; H, 6.44.

Benzyl (2-cyanomethyl)-5-phenylpent-2-enoate [4ba, a mixture of stereoisomers (*Z*/*E* = 91 : 9)]. A colorless oil, R_f 0.13 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–6.96 (m, 10.09H), 7.37 (tt, *J* = 7.5, 1.3 Hz, 0.91H), 5.12 (s, 0.18H), 5.10 (s, 1.82H), 3.23 (d, *J* = 1.3 Hz, 1.82H), 3.14 (s, 0.18H), 2.82 (td, *J* = 8.1, 7.5 Hz, 1.82H), 2.70 (t, *J* = 7.7 Hz, 0.18H), 2.64 (t, *J* = 8.1 Hz, 1.82H), 2.49 (q, *J* = 7.7 Hz, 0.18H); ^{13}C NMR [for (*Z*)-4ba, 101 MHz, $CDCl_3$] δ 164.6, 147.7, 140.6, 135.2, 128.7, 128.6, 128.5,

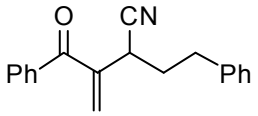
128.4, 128.3, 126.1, 121.4, 117.2, 67.0, 34.8, 31.3, 22.6; IR [neat, as a mixture with (*E*)-**4ba**] 3028, 2930, 2253, 1707, 1497, 1454, 1215, 1113, 750, 698 cm^{-1}. Anal. Calcd for $C_{20}H_{19}NO_2$; C, 78.66; H, 6.27. Found: C, 78.64; H, 6.35.

Ethyl 3-cyano-3-methyl-2-methylenebutanoate (3al). A colorless oil, R_f 0.30 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.36 (s, 1H), 5.96 (s, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.65 (s, 6H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 140.6, 126.1, 123.4, 61.3, 35.6, 26.7, 14.1; IR (neat) 2986, 2238, 1720, 1624, 1466, 1367, 1313, 1213, 1111, 1024, 964, 814 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_2$; C, 64.65; H, 7.84. Found: C, 64.38; H, 7.84.

Ethyl 2-(cyanomethyl)-3-methylbut-2-enoate (4al). A colorless oil, R_f 0.28 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 4.24 (q, *J* = 7.1 Hz, 2H), 3.38 (s, 2H), 2.20 (s, 3H), 1.99 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 153.3, 117.6, 116.9, 60.9, 23.9, 23.5, 18.2, 14.2; IR (neat) 2984, 2249, 1715, 1639, 1371, 1283, 1205, 1078, 1020 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_2$; C, 64.65; H, 7.84. Found: C, 64.71; H, 8.12.

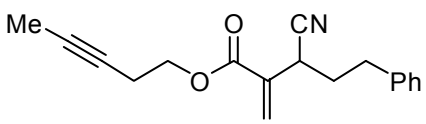
Ethyl (*Z*)-2-(1-cyanopent-1-yl)hept-2-enoate (3am). A colorless oil, R_f 0.35 (hexane–ethyl acetate = 10 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 6.39 (t, *J* = 7.5 Hz, 1H), 4.31–4.18 (m, 2H), 3.72 (dd, *J* = 8.8, 5.6 Hz, 1H), 2.62–2.46 (m, 2H), 1.80–1.60 (m, 2H), 1.56–1.24 (m, 8H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 146.4, 126.9, 120.5, 61.0, 35.2, 33.1, 31.1, 29.4, 29.0, 22.4, 22.0, 14.2, 13.8, 13.7; IR (neat) 2959, 2862, 2241, 1722, 1641, 1466, 1383, 1229, 1148 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NO_2$; C, 71.67; H, 10.02. Found: C, 71.39; H, 9.85.

Benzoylcyanation of 5-phenyl-1,2-pentadiene (2a). In a dry box, benzyol cyanide (**11**, 131 mg, 1.00 mmol) and 5-phenyl-1,2-pentadiene (**2a**, 288 mg, 2.0 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and $PMePh_2$ (40 mg, 0.20 mmol) in toluene (2.0 mL) placed in a vial. The vial was closed and taken outside the dry box, and heated at 70 °C for 60 h. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography followed by preparative GPC to give 3-benzoyl-2-(2-phenylethyl)-3-butenenitrile (**12**, 129 mg, 47%) as a colorless oil, R_f 0.25 (hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.76–7.68 (m, 2H), 7.63–7.56 (m, 1H), 7.52–7.43 (m, 2H), 7.36–7.27 (m, 2H), 7.25–7.17 (m, 3H), 6.42 (s, 1H), 5.60 (s, 1H), 4.12 (dd, J = 9.3, 4.2 Hz, 1H), 2.90–3.00 (m, 1H), 2.88–2.78 (m, 1H), 2.19–1.96 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.7, 142.4, 139.6, 136.6, 133.0, 129.5, 129.0, 128.6, 128.5, 128.4, 126.5, 119.8, 34.1, 33.4, 33.3; IR (neat) 3028, 2928, 2241, 1659, 1597, 1448, 1263, 984, 752, 698 cm^{-1}. Anal. Calcd for $C_{19}H_{17}NO$; C, 82.88; H, 6.22. Found: C, 82.74; H, 6.28.



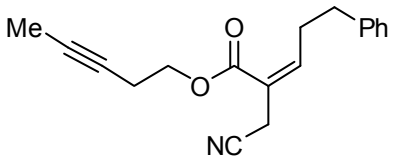
Nickel-catalyzed three-component cyanoesterificaction of 1,2-dienes. ***A general procedure.*** In a dry box, chloroformate ester (1.10 mmol), trimethylsilyl cyanide (109 mg, 1.10 mmol), and a 1,2-diene (1.00 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and dppp (41 mg, 0.100 mmol) in toluene (0.67 mL) placed in a vial. The vial was closed and taken outside the dry box, and heated at 60 °C for the time specified in Tables 4 and 5. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give the corresponding cyanoesterification products in yields listed in Tables 4 and 5.

Pent-3-yn-1-yl 3-cyano-2-methylene-5-phenylpentanoate (15ba). A colorless oil, R_f 0.53 (hexane–ethyl acetate = 3 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.28 (m, 3H), 7.25–7.18 (m, 2H), 6.50 (s, 1H), 6.10 (d, J = 1.1 Hz, 1H), 4.30–4.16 (m, 2H), 3.78 (dd, J = 4.8, 9.5 Hz, 1H), 2.96–2.72 (m, 2H), 2.54–2.44 (m, 2H), 2.24–1.96 (m, 2H), 1.74 (t, J = 2.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2,



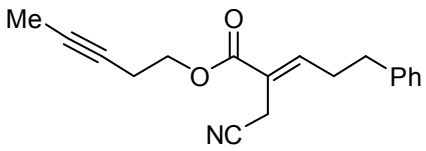
139.6, 135.3, 128.6, 128.5, 128.4, 126.5, 119.5, 77.6, 74.3, 63.8, 34.2, 33.2, 33.1, 19.1, 3.4; IR (neat) 3063, 3028, 2961, 2920, 2861, 2243, 1721, 1632, 1603, 1497, 1454, 1412, 1343, 1325, 1287, 1258, 1238, 1169, 1140, 1030, 1007, 963, 814, 750, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{19}NO_2$; C, 76.84; H, 6.81. Found: C, 76.85; H, 6.84.

Pent-3-yn-1-yl (*Z*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-16ba]. A colorless



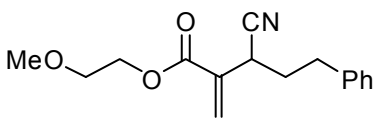
oil, R_f 0.43 (hexane–ethyl acetate = 3 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.24–7.18 (m, 3H), 6.49 (tt, *J* = 7.4, 1.4 Hz, 1H), 4.24 (t, *J* = 6.7 Hz, 2H), 3.35 (q, *J* = 1.3 Hz, 2H), 2.97 (q, *J* = 7.3 Hz, 2H), 2.79 (t, *J* = 7.7 Hz, 2H), 2.56–2.48 (m, 2H), 1.71 (t, *J* = 2.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 147.6, 140.7, 128.5, 128.4, 126.2, 121.5, 117.2, 77.6, 74.5, 63.5, 34.9, 31.2, 22.6, 19.2, 3.3; IR (neat) 3026, 2961, 2920, 2859, 2253, 1722, 1713, 1649, 1603, 1497, 1454, 1416, 1393, 1373, 1339, 1261, 1213, 1180, 1117, 1072, 1007, 883, 864, 829, 750, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{19}NO_2$; C, 76.84; H, 6.81. Found: C, 76.61; H, 6.78.

Pent-3-yn-1-yl (*E*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*E*)-16ba]. A colorless



oil, R_f 0.40 (hexane–ethyl acetate = 3 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.26–7.16 (m, 3H), 7.11 (t, *J* = 7.7 Hz, 1H), 4.25 (t, *J* = 6.9 Hz, 2H), 3.35 (s, 2H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.61 (q, *J* = 7.6 Hz, 2H), 2.56–2.48 (m, 2H), 1.78 (t, *J* = 2.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 146.8, 140.1, 128.6, 128.3, 126.5, 122.6, 116.8, 77.5, 74.3, 63.7, 34.1, 31.0, 19.2, 15.0, 3.4; IR (neat) 3028, 2959, 2920, 2859, 2251, 1713, 1651, 1603, 1497, 1454, 1418, 1389, 1339, 1279, 1209, 1105, 1076, 1055, 1030, 1003, 978, 920, 748, 700 cm^{-1}. Anal. Calcd for $C_{18}H_{19}NO_2$; C, 76.84; H, 6.81. Found: C, 76.88; H, 6.91.

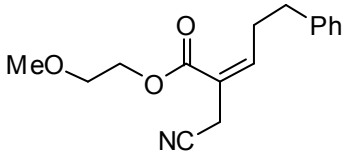
2-Methoxyethyl 3-cyano-2-methylene-5-phenylpentanoate (15ca). A colorless oil, R_f



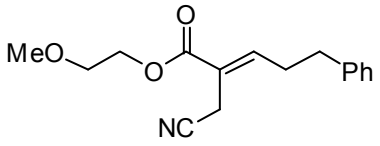
0.35 (hexane–ethyl acetate = 4 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.27 (m, 3H), 7.25–7.17 (m, 2H), 6.51 (s, 1H), 6.10 (d, *J* = 1.1 Hz, 1H), 4.39–4.28 (m, 2H), 3.78

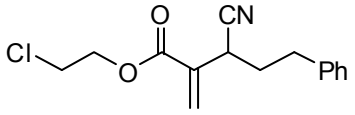
(ddd, J = 9.3, 4.8, 0.7 Hz, 1H), 3.62 (t, J = 4.8 Hz, 2H), 3.38 (s, 3H), 2.95–2.85 (m, 1H), 2.83–2.73 (m, 1H), 2.21–2.10 (m, 1H), 2.07–1.96 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 139.6, 135.3, 128.6, 128.5, 128.4, 126.5, 119.5, 70.1, 64.5, 59.0, 34.2, 33.2, 33.1; IR (neat) 3028, 2930, 2893, 2823, 2243, 1721, 1632, 1603, 1497, 1454, 1412, 1373, 1344, 1287, 1260, 1200, 1128, 1032, 963, 912, 868, 841, 814, 752, 700 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{19}NO_3$: M^+, 273.1365. Found: m/z 273.1370.

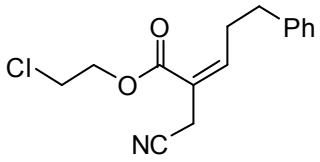
2-Methoxyethyl (*Z*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-16ca]. A colorless oil, R_f 0.29 (hexane–ethyl acetate = 4 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 2H), 7.24–7.18 (m, 3H), 6.48 (tt, J = 7.3, 1.3 Hz, 1H), 4.33 (t, J = 4.7 Hz, 2H), 3.63 (t, J = 4.8 Hz, 2H), 3.38–3.33 (m, 5H), 2.95 (qd, J = 7.9, 0.9 Hz, 2H), 2.79 (t, J = 8.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.8, 147.6, 140.7, 128.5, 128.4, 126.2, 121.5, 117.2, 70.2, 64.0, 58.9, 34.9, 31.2, 22.6; IR (neat) 2926, 2895, 2818, 2253, 1707, 1655, 1647, 1603, 1497, 1454, 1414, 1389, 1217, 1117, 1030, 868, 750, 702 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{19}NO_3$: M^+, 273.1365. Found: m/z 273.1356.

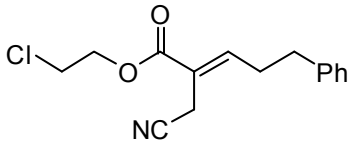


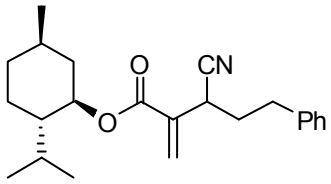
2-Methoxyethyl (*E*)-(2-cyanomethyl)-5-phenyl-2-pentenoate [(*E*)-16ca]. A colorless oil, R_f 0.23 (hexane–ethyl acetate = 4 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.26–7.16 (m, 3H), 7.12 (t, J = 7.7 Hz, 1H), 4.33 (t, J = 4.7 Hz, 2H), 3.65 (t, J = 4.7 Hz, 2H), 3.39 (s, 3H), 3.25 (s, 2H), 2.83 (t, J = 7.5 Hz, 2H), 2.60 (q, J = 7.7 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 146.9, 140.1, 128.6, 128.3, 126.5, 122.5, 116.8, 70.3, 64.5, 59.0, 34.1, 31.1, 15.0; IR (neat) 3028, 2934, 2895, 2251, 1713, 1651, 1603, 1497, 1454, 1410, 1377, 1287, 1248, 1213, 1128, 1107, 1061, 1030, 922, 866, 750, 702 cm^{-1}; HRMS (EI) Calcd for $C_{16}H_{19}NO_3$: M^+, 273.1365. Found: m/z 273.1368.



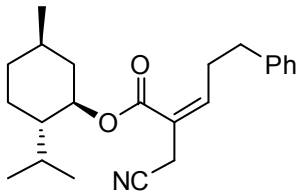
2-Chloroethyl 3-cyano-2-methylene-5-phenylpentanoate (15da). A colorless oil, R_f 0.41 (hexane–ethyl acetate = 3 : 1).  ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.28 (m, 3H), 7.26–7.18 (m, 2H), 6.54 (s, 1H), 6.13 (d, *J* = 1.1 Hz, 1H), 4.50–4.37 (m, 2H), 3.80–3.67 (m, 3H), 2.98–2.86 (m, 1H), 2.85–2.72 (m, 1H), 2.23–2.11 (m, 1H), 2.10–1.94 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0, 139.5, 135.0, 129.1, 128.6, 128.4, 126.5, 119.3, 64.9, 41.3, 34.2, 33.2, 33.1; IR (neat) 3063, 3028, 2928, 2864, 2245, 1719, 1630, 1603, 1497, 1454, 1412, 1387, 1304, 1256, 1140, 1018, 964, 814, 750, 700, 667 cm^{-1}. Anal. Calcd for $C_{15}H_{16}ClNO_2$; C, 64.87; H, 5.81. Found: C, 64.66; H, 5.88.

2-Chloroethyl (*Z*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-16da]. A pale yellow oil, R_f 0.35 (hexane–ethyl acetate = 3 : 1).  ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.24–7.18 (m, 3H), 6.53 (tt, *J* = 7.4, 1.4 Hz, 1H), 4.41 (t, *J* = 5.5 Hz, 2H), 3.73 (t, *J* = 5.5 Hz, 2H), 3.37 (q, *J* = 1.3 Hz, 2H), 2.98 (q, *J* = 7.6 Hz, 2H), 2.81 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 148.4, 140.4, 128.4, 128.3, 126.1, 121.0, 117.0, 64.6, 41.5, 34.9, 31.4, 22.7; IR (neat) 3061, 3026, 2930, 2861, 2255, 1726, 1711, 1647, 1603, 1497, 1454, 1433, 1414, 1393, 1302, 1215, 1179, 1117, 1074, 1013, 910, 750, 735, 700, 667 cm^{-1}; Anal. Calcd for $C_{15}H_{16}ClNO_2$; C, 64.87; H, 5.81. Found (as a mixture with (*E*)-**16da**): C, 64.91; H, 5.88.

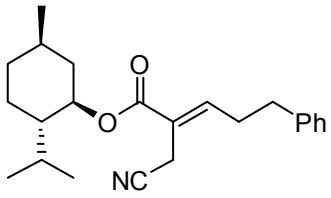
2-Chloroethyl (*E*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*E*)-16da]. A pale yellow oil, R_f 0.33 (hexane–ethyl acetate = 3 : 1).  ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.28 (m, 2H), 7.17–7.12 (m, 3H), 7.15 (t, *J* = 7.7 Hz, 1H), 4.45 (t, *J* = 5.7 Hz, 2H), 3.75 (t, *J* = 5.6 Hz, 2H), 3.25 (s, 2H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.63 (q, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 147.4, 139.8, 128.6, 128.2, 126.4, 122.1, 116.6, 64.9, 41.5, 34.2, 31.3, 15.2; IR (neat) 3028, 2943, 2862, 2253, 1713, 1651, 1603, 1497, 1454, 1433, 1414, 1387, 1306, 1283, 1211, 1111, 1078, 1051, 912, 733, 700, 667 cm^{-1}.

(–)-Menthyl 3-cyano-2-methylene-5-phenylpentanoate [15ea, a mixture of diastereoisomers (50 : 50)]. 

A colorless oil, R_f 0.44 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$, as a mixture of diastereoisomers) δ 7.36–7.27 (m, 2H), 7.26–7.15 (m, 3H), 6.44 (d, *J* = 0.5 Hz, 1H), 6.05 (t, *J* = 1.1 Hz, 1H), 4.83–4.72 (m, 1H), 3.81–3.74 (m, 1H), 2.95–2.85 (m, 1H), 2.82–2.72 (m, 1H), 2.20–1.92 (m, 3H), 1.90–1.64 (m, 3H), 1.57–1.32 (m, 2H), 1.14–0.82 (m, 9H), 0.76 (d, *J* = 6.8 Hz, 1.5H), 0.74 (d, *J* = 7.0 Hz, 1.5H); ^{13}C NMR (101 MHz, $CDCl_3$, as a mixture of diastereoisomers) δ 164.00, 163.98, 139.67, 139.65, 135.9, 128.63, 128.62, 128.43, 128.40, 127.7, 127.6, 126.48, 126.45, 119.64, 119.60, 75.7, 47.0, 46.9, 40.7, 40.6, 34.4, 34.11, 34.08, 33.24, 33.21, 33.08, 33.07, 31.4, 26.5, 26.4, 23.5, 23.3, 21.9, 20.7, 20.6, 16.4, 16.2; IR (neat, as a mixture of diastereoisomers) 3412, 3028, 3000, 2928, 2870, 2243, 1711, 1636, 1497, 1456, 1389, 1369, 1344, 1258, 1140, 1038, 957, 918, 814, 748, 700 cm^{-1}; HRMS (EI) Calcd for $C_{23}H_{31}NO_2$: M^+, 353.2355. Found: *m*/*z* 353.2338.

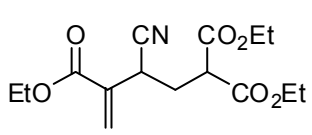
(–)-Menthyl (*Z*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*Z*)-16ea]. 

A colorless oil, R_f 0.33 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 2H), 7.25–7.17 (m, 3H), 6.42 (tt, *J* = 7.5, 1.5 Hz, 1H), 4.81 (td, *J* = 10.8, 4.6 Hz, 1H), 3.32 (t, *J* = 1.3 Hz, 2H), 3.00–2.87 (m, 2H), 2.78 (t, *J* = 7.7 Hz, 2H), 2.07–1.97 (m, 1H), 1.93–1.78 (m, 1H), 1.75–1.65 (m, 2H), 1.55–1.38 (m, 2H), 1.15–0.96 (m, 2H), 0.93–0.86 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.5, 146.7, 140.8, 128.5, 128.4, 126.2, 122.0, 117.3, 75.4, 47.0, 40.9, 35.0, 34.1, 31.4, 31.2, 26.3, 23.2, 22.7, 22.0, 20.8, 16.1; IR (neat) 2957, 2928, 2870, 2255, 1722, 1715, 1705, 1699, 1603, 1497, 1454, 1416, 1387, 1371, 1261, 1217, 1180, 1119, 1098, 1080, 1038, 1009, 982, 961, 914, 845, 750, 700 cm^{-1}; HRMS (EI) Calcd for $C_{23}H_{31}NO_2$: M^+, 353.2355. Found: *m*/*z* 353.2363.

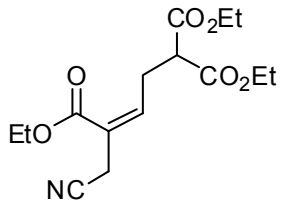
(–)-Menthyl (*E*)-(2-cyanomethyl)-5-phenylpent-2-enoate [(*E*)-16ea]. A colorless oil, 

R_f 0.29 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.26 (m, 2H), 7.25–7.15 (m, 3H), 7.05 (t, *J* = 7.7 Hz, 1H), 4.78 (td, *J* = 11.0, 4.4 Hz, 1H), 3.26 (d, *J* = 17.6 Hz, 1H), 3.20 (d, *J* = 17.7 Hz, 1H), 2.83 (t, *J* = 7.3 Hz, 2H), 2.59 (q, *J* = 7.9 Hz, 2H), 2.08–1.98 (m, 1H), 1.91–1.78 (m, 1H), 1.75–1.64 (m, 2H), 1.57–1.40 (m, 2H), 1.15–0.98 (m, 2H), 0.96–0.83 (m, 1H), 0.92 (d, *J* = 2.6 Hz, 3H), 0.91 (d, *J* = 3.1 Hz, 3H), 0.77 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 145.9, 140.1, 128.6, 128.3, 126.4, 123.1, 117.0, 75.6, 47.1, 40.7, 34.22, 34.15, 31.4, 31.0, 26.4, 23.4, 22.0, 20.7, 16.4, 15.0; IR (neat) 3028, 2955, 2928, 2870, 2251, 1701, 1655, 1497, 1454, 1369, 1277, 1213, 1180, 1099, 1051, 982, 962, 916, 847, 746, 700 cm^{-1}; HRMS (EI) Calcd for $C_{23}H_{31}NO_2$: M^+, 353.2355. Found: *m*/*z* 353.2351.

Triethyl 3-cyanopent-1-ene-1,1,4-tricarboxylate (3an). A colorless oil, R_f 0.53 (hexane–ethyl acetate = 3 :1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (s, 1H), 6.03 (s, 1H), 4.28–4.12 (m, 6H), 3.93 (dd, *J* = 9.0, 5.3 Hz, 1H), 3.53 (t, *J* = 7.4 Hz, 1H), 2.45–2.24 (m, 2H), 1.34–1.20 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.96, 167.93, 164.0, 134.8, 128.7, 118.6, 61.9, 61.8, 61.7, 49.3, 31.6, 31.2, 13.96, 13.88, 13.85; IR (neat) 2984, 2939, 2245, 1732, 1636, 1447, 1394, 1371, 1254, 1177, 1151, 1097, 1026, 968, 862, 814 cm^{-1}; HRMS (EI) Calcd for $C_{15}H_{21}NO_6$: M^+, 311.1369. Found: *m*/*z* 311.1361.



Triethyl (*Z*)-5-cyanopent-3-ene-1,1,4-tricarboxylate [(*Z*)-4an]. A colorless oil, R_f 0.40 (hexane–ethyl acetate = 3 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.42 (t, *J* = 7.3 Hz, 1H), 4.32–4.14 (m, 6H), 3.52 (t, *J* = 7.3 Hz, 1H), 3.34 (d, *J* = 1.1 Hz, 2H), 3.16 (t, *J* = 7.3 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 164.5, 143.0, 123.5, 116.9, 61.7, 61.4, 51.0, 28.5, 22.6, 14.1, 14.0; IR (neat) 2984, 2941, 2916, 2255, 1732, 1653, 1447, 1420, 1371, 1339, 1227, 1180, 1113, 1097, 1034, 860 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_6$; C, 57.87; H, 6.80. Found: C, 57.88; H, 6.69.



Triethyl (*E*)-5-cyanopent-3-ene-1,1,4-tricarboxylate [(*E*)-4an]. A colorless oil, R_f 0.40 (hexane–ethyl acetate = 3 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (t, *J* = 7.9 Hz, 1H), 4.30–4.14 (m, 6H), 3.52 (t, *J* = 7.3 Hz, 1H), 3.46 (s, 2H), 2.84 (t, *J* = 7.5 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 164.8, 142.1, 124.8, 116.8, 62.0, 61.7, 50.3, 28.1, 15.2, 14.1, 14.0; IR (neat) 2984, 2939, 2914, 2253, 1732, 1713, 1657, 1466, 1447, 1414, 1393, 1371, 1267, 1213, 1180, 1159, 1115, 1096, 1057, 1034, 860, 758 cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_6$; C, 57.87; H, 6.80. Found: C, 58.10; H, 6.73.

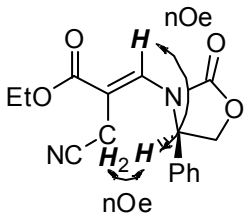
Ethyl 2-[cyano(phenyl)methyl]acrylate (3ao). A colorless oil, R_f 0.46 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.28 (m, 5H), 6.51 (s, 1H), 6.07 (d, *J* = 1.1 Hz, 1H), 5.07 (s, 1H), 4.27–4.13 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.2, 136.3, 133.6, 129.0, 128.5, 128.2, 127.9, 118.7, 61.6, 38.8, 13.9; IR (neat) 2984, 2916, 2849, 2243, 1717, 1636, 1493, 1454, 1412, 1369, 1321, 1258, 1142, 1042, 964, 912, 760, 700 cm^{-1}; HRMS (EI) Calcd for $C_{13}H_{13}NO_2$: M^+, 215.0946. Found: *m*/*z* 215.0947.

Ethyl (*Z*)-(2-cyanomethyl)-3-phenylacrylate [(*Z*)-4ao]. A colorless oil, R_f 0.29 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 7.24 (s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.53 (d, *J* = 1.6 Hz, 2H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 140.4, 134.8, 128.7, 128.6, 128.0, 122.5, 116.7, 61.4, 23.1, 13.6; IR (neat) 2984, 2916, 2849, 2255, 1707, 1410, 1381, 1215, 1101, 1018, 746, 696 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_2$; C, 72.54; H, 6.09. Found : C, 72.62; H, 6.15.

Ethyl (*E*)-(2-cyanomethyl)-3-phenylacrylate [(*E*)-4ao]. A colorless oil, R_f 0.38 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.50–7.37 (m, 5H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.52 (d, *J* = 0.7 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 143.7, 133.8, 129.7, 129.1, 129.0, 122.2, 117.4, 61.8, 16.9, 14.2; IR (neat) 2984, 2916,

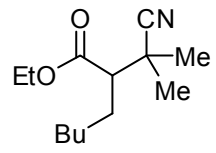
2849, 2251, 1707, 1638, 1448, 1373, 1271, 1225, 1096, 1020, 766, 702 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO_2$; C, 72.54; H, 6.09. Found : C, 72.72; H, 6.09.

Ethyl (*R*,*Z*)-(2-cyanomethyl)-3-(2-oxo-4-phenyl-oxazoline-3-yl)acrylate [(*Z*)-4ap]. A



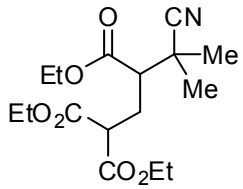
colorless oil, R_f 0.27 (hexane–ethyl acetate = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 0.9 Hz, 1H), 7.51–7.35 (m, 3H), 7.34–7.21 (m, 2H), 5.40 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.80 (t, *J* = 8.6 Hz, 1H), 4.30–4.14 (m, 3H), 3.49 (d, *J* = 17.7 Hz, 1H), 3.14 (dd, *J* = 17.9, 1.3 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 154.9, 137.4, 135.7, 130.0, 129.7, 125.3, 117.3, 106.6, 70.8, 61.7, 59.8, 15.3, 14.1; IR (neat) 2982, 2916, 2849, 2251, 1778, 1703, 1651, 1475, 1458, 1391, 1367, 1271, 1182, 1132, 1092, 1080, 1040, 941, 907, 866, 760, 729, 702 cm^{-1}. Anal. Calcd for $C_{16}H_{16}N_2O_4$; C, 63.99; H, 5.37. Found : C, 63.69; H, 5.42.

1,4-Addition of *n*-BuCu•BF_3 to 3al. To a suspension of CuI (3.0 g, 16.0 mmol) in diethyl ether (24 mL) was added a 1.6 M solution of *n*-BuLi in hexane (10 mL, 16.0 mmol) at –40 °C. To this was added dropwise BF_3•Et_2O (2.0 mL, 16.0 mmol) and **3al** (0.67 g, 4.0 mmol) sequentially at –70 °C, and the resulting mixture was stirred at –70 °C for 2 h and then at room temperature for 5 h before quenching with a saturated NH_4Cl aqueous solution. The organic layer was separated, and the aqueous layer was extracted with diethyl ether for three times. The combined organic layer was washed with water for six times and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give ethyl 2-(2-cyanoprop-2-yl)heptanoate (**28a**, 0.74 g, 82%) as a colorless oil, R_f 0.24

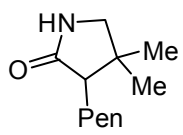


(hexane–ethyl acetate = 10 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.19 (q, *J* = 7.1 Hz, 2H), 2.38 (dd, *J* = 11.9, 3.3 Hz, 1H), 1.90–1.77 (m, 1H), 1.70–1.58 (m, 1H), 1.40 (s, 3H), 1.38 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.36–1.18 (m, 6H), 0.87 (t, *J* = 5.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 123.5, 60.8, 53.6, 34.5, 31.4, 28.7, 27.2, 26.0, 24.0, 22.3, 14.2, 13.9; IR (neat) 2957, 2235, 1734, 1466, 1375, 1258, 1178, 1144, 1026 cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_2$; C, 62.29; H, 10.29. Found: C, 62.32; H, 10.04.

1,4-Addition of diethyl malonate to 3al. A solution of sodium malonate was prepared by treatment of diethyl malonate (34 mg, 0.21 mmol) with NaH (6.2 mg, 0.26 mmol) at 0 °C in THF (0.4 mL). To a solution of **3al** (33 mg, 0.20 mmol) in THF (0.40 mL) was added the solution of sodium malonate at 0 °C, and the resulting mixture was stirred at room temperature for 1 h, before quenching with a few drops of water and was filtered through a pad of anhydrous $MgSO_4$. The residue was purified by flash column chromatography on silica gel to give ethyl triethyl 4-cyano-4-methylpentane-1,1,3-tricarboxylate (**28b**, 49 mg, 74%) as a colorless oil, R_f 0.13 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28–4.10 (m, 6H), 3.27 (dd, *J* = 10.3, 4.9 Hz, 1H), 2.47 (dd, *J* = 10.9, 4.1 Hz, 1H), 2.38–2.23 (m, 2H), 1.44 (s, 3H), 1.39 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 168.3, 122.7, 61.8, 61.7, 61.3, 51.0, 49.8, 34.4, 27.5, 25.5, 24.6, 14.1, 14.0, 13.9; IR (neat) 2984, 2237, 1732, 1468, 1447, 1371, 1246, 1177, 1038, 854 cm^{-1}. Anal. Calcd for $C_{16}H_{25}NO_5$; C, 58.70; H, 7.70. Found: C, 58.68; H, 7.59.



γ-Lactam synthesis from 28a. To a solution of **28a** (113 mg, 0.50 mmol) and $CoCl_2$ (130 mg, 1.00 mmol) in EtOH (14.0 mL) was added $NaBH_4$ (189 mg, 5.0 mmol) portionwise at 0 °C, the resulting mixture was stirred at 0 °C for 1.5 h and then at room temperature overnight before quenching with a 1 M HCl aqueous solution and the mixture was stirred at room temperature for 0.5 h. After neutralization with a saturated $NaHCO_3$ aqueous solution, the organic layer was separated, and the aqueous layer was extracted with diethyl ether three times. The combined organic layers were washed with water for three times and brine, dried withr anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to give 4,4-dimethyl-3-pentylpyrrolidin-2-one (**29**, 59 mg, 64%) as a white solid mp 88.6–89.2 °C, R_f 0.13 (hexane–ethyl acetate = 5 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.31 (br s, 1H), 3.03 (d, *J* = 9.3 Hz, 1H), 2.95 (d, *J* = 9.3 Hz, 1H), 1.98 (t, *J* = 6.8 Hz, 1H), 1.68–1.50 (m, 2H), 1.48–1.22 (m, 6H), 1.15 (s, 3H), 0.99 (s, 3H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.3, 54.2,



51.5, 39.5, 32.1, 28.0, 27.2, 25.6, 22.5, 22.0, 14.1; IR (KBr) 3201, 3091, 2956, 2930, 2870, 1707, 1682, 1465, 1321, 1078, 797, 706, 581, 542 cm^{-1}. Anal. Calcd for $C_{11}H_{21}NO$; C, 72.08; H, 11.55. Found: C, 71.78; H, 11.47.

Carbocyanation of 4-octyne using 3aa. In a dry box, **3aa** (1.00 mmol) and 4-octyne (165 mg, 1.50 mmol) were added to a solution of $Ni(cod)_2$ (28 mg, 0.100 mmol) and P(4-CF_3–C_6H_4)$_3$ (92 mg, 0.20 mmol) in CH_3CN (2.0 mL) placed in a vial. The vial was closed and taken outside the dry box, and heated at 80 °C for 8 h. The resulting mixture was filtered through a silica gel pad, concentrated *in vacuo*, and purified by flash silica gel column chromatography to give ethyl (2*E*,4*Z*)-5-cyano-(3-phenyl-1-propylidene)-4-propyloct-4-enoate [**30**, mixture of stereoisomers (2*E*:2*Z* = 83:17), 288 mg, 81%] as a colorless oil,. Stereoisomers were further separated by preparative recycling silica gel chromatography.

(2*E*)-30. R_f 0.41(hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.15 (m, 5H), 6.99 (t, *J* = 7.5 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.47 (s, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 2.56 (q, *J* = 7.5 Hz, 2H), 2.17 (t, *J* = 7.3 Hz, 2H), 1.96 (t, *J* = 8.1 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.40–1.25 (m, 5H), 0.93 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 156.3, 144.8, 140.7, 129.0, 128.5, 128.3, 126.2, 119.2, 111.2, 60.8, 34.7, 33.3, 32.4, 31.7, 30.6, 21.8, 21.6, 14.2, 13.5; IR (neat) 2963, 2206, 1713, 1643, 1454, 1277, 1120, 1053, 914, 765, 700 cm^{-1}; HRMS (EI) Calcd for $C_{23}H_{31}NO_2$: M^+, 353.2355. Found: *m*/*z* 353.2364.

(2*Z*)-30. R_f 0.41(hexane–ethyl acetate = 5 : 1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.24 (m, 2H), 7.22–7.14 (m, 3H), 5.94 (t, *J* = 7.3 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.35 (s, 2H), 2.88–2.70 (m, 4H), 2.18 (t, *J* = 7.3 Hz, 2H), 2.00 (t, *J* = 7.9 Hz, 2H), 1.56 (sext, *J* = 7.5 Hz, 2H), 1.40–1.26 (m, 5H), 0.94 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 156.2, 143.7, 141.1, 128.8, 128.44, 128.36, 126.0, 119.1, 112.1, 60.5, 40.1, 35.2, 32.5, 31.7, 31.0, 21.7, 21.3, 14.2, 14.1, 13.5; IR (neat) 2963, 2206,

1713, 1643, 1454, 1277, 1200, 1053, 735, 700 cm^{-1}. HRMS (EI) Calcd for $C_{23}H_{31}NO_2$: M^+, 353.2355. Found: *m*/*z* 353.2357.

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List of Publications

I. Parts of the present Thesis have been or are to be published in the following journals.

Chapter 2

Allylcyanation of Alkynes: Regio- and Stereoselective Access to Functionalized Di- or Trisubstituted Acrylonitriles

Nakao, Y.; Yukawa, T.; Hirata, Y.; Oda, S.; Sato, J.; Hiyama, T. *J. Am. Chem. Soc*. **2006**, *128*, 7116–7117.

Allylcyanation of Alkynes Catalyzed by Nickel

Hirata, Y.; Yukawa, T.; Kashihara, N.; Nakao, Y.; Hiyama, T. in preparation.

Chapter 3

Nickel/BPh_3-Catalyzed Alkynylcyanation of Alkynes and 1,2-Dienes: An Efficient Route to Highly Functionalized Conjugated Enynes

Nakao, Y.; Hirata, Y.; Tanaka, M.; Hiyama, T. *Angew. Chem. Int. Ed*. **2008**, *47*, 385–387.

Alkynylcyanation of Alkynes and Dienes Catalyzed by Nickel

Hirata, Y.; Tanaka, M.; Nakao, Y.; Hiyama, T. in preparation.

Chapter 4

Nickel/Lewis Acid-Catalyzed Cyanoesterification and Cyanocarbamoylation of Alkynes

Hirata, Y.; Nakao, Y.; Hiyama, T. in preparation.

Chapter 5

Cyanoesterification of 1,2-Dienes: Synthesis and Transformations of Highly Functionalized α-Cyanomethylacrylate Esters

Nakao, Y.; Hirata, Y.; Hiyama, T. *J. Am. Chem. Soc*. **2006**, *128*, 7420–7421.

Cyanoesterification of 1,2-Dienes Catalyzed by Nickel
Hirata, Y.; Inui, T.; Nakao, Y.; Hiyama, T. in preparation.

II. Following publication is not included in this Thesis.

Stannylative Cycloaddition of Enynes Catalyzed by Palladium–Iminophosphine
Nakao, Y.; Hirata, Y.; Ishihara, S.; Oda, S.; Yukawa, T.; Shirakawa, E.; Hiyama, T. *J. Am. Chem. Soc*. **2004**, *126*. 15650–15651.

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